# TREATMENT OF MULTIPLE WARTS – EFFICACY OF HOMOLOGOUS AUTOIMPLANTATION THERAPY & COMPARISON OF HOMOLOGOUS AUTOIMPLANTION THERAPY & CRYOTHERAPY WITH LIQUID NITROGEN

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**(BRANCH XX)**


**MADRAS MEDICAL COLLEGE**

**THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY**
**CHENNAI, INDIA.**

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# CERTIFICATE

Certified that this dissertation titled **"TREATMENT OF MULTIPLE WARTS – EFFICACY OF HOMOLOGOUS AUTOIMPLANTATION THERAPY & COMPARISON OF HOMOLOGOUS AUTOIMPLANTION THERAPY & CRYOTHERAPY WITH LIQUID NITROGEN"** is a bonafide work done by **Dr.V.SUGANTHY,** Post graduate student of the Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 3, during the academic year 2010 – 2013. This work has not previously formed the basis for the award of any degree.

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# DECLARATION

I, **Dr.V.SUGANTHY,** solemnly declare that this dissertation titled **"TREATMENT OF MULTIPLE WARTS – EFFICACY OF HOMOLOGOUS AUTO IMPLANTATION THERAPY & COMPARISON OF HOMOLOGOUS AUTOIMPLANTION THERAPY & CRYOTHERAPY WITH LIQUID NITROGEN"** is a bonafide work done by me at Madras Medical College during 2010-2013 under the guidance and supervision of **Prof.Dr.K.MANOHARAN, M.D.,D.D.,** Professor and head of the department of Dermatology, Madras Medical College,Chennai-600003.

This dissertation is submitted to The Tamil Nadu Dr.M.G.R.Medical University, Chennai towards partial fulfillment of the rules and regulations for the award of **M.D Degree in Dermatology, Venereology and Leprology (BRANCH – XX)**

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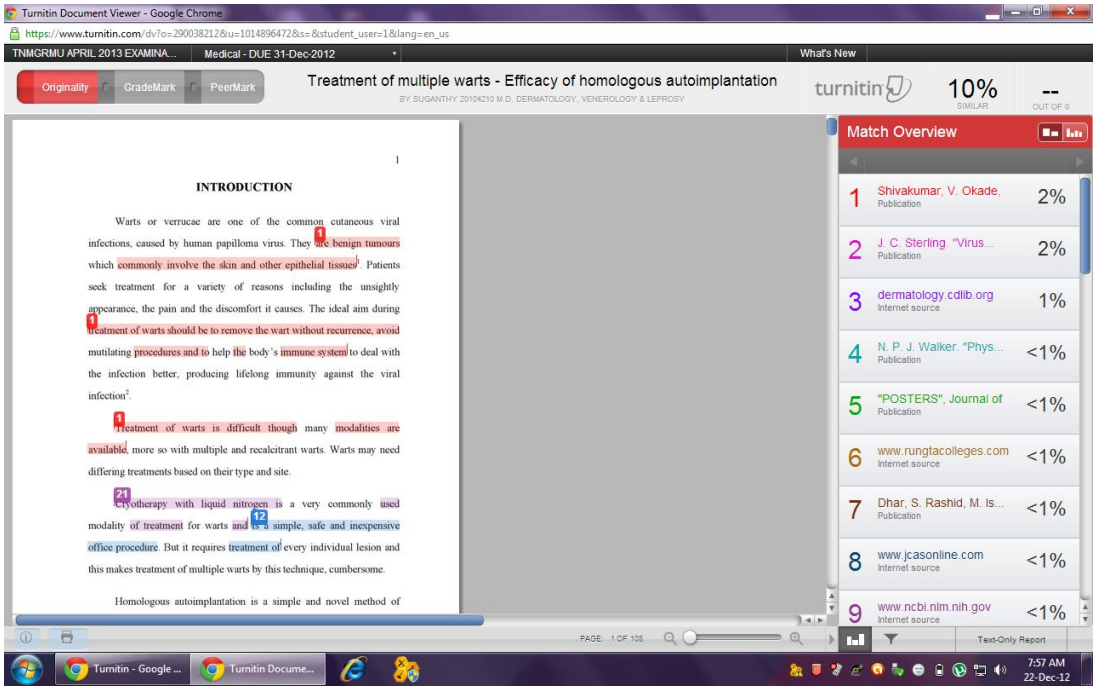
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Treatment of multiple warts - Efficacy of homologous autoimplantation
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INTRODUCTION
Warts or verrucae are one of the common cutaneous viral infections, caused by human papilloma virus. They are benign tumours which commonly involve the skin and other epithelial tissues[1]. Patients seek treatment for a variety of reasons including the unsightly appearance, the pain and the discomfort it causes. The ideal aim during treatment of warts should be to remove the wart without recurrence, avoid mutilating procedures and to help the body's immune system to deal with the infection better, producing lifelong immunity against the viral infection[2].
Treatment of warts is difficult though many modalities are available, more so with multiple and recalcitrant warts. Warts may need differing treatments based on their type and site.
Cryotherapy with liquid nitrogen is a very commonly used modality of treatment for warts and is a simple, safe and inexpensive office procedure. But it requires treatment of every individual lesion and this makes treatment of multiple warts by this technique, cumbersome.
Homologous autoimplantation is a simple and novel method of
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# INTRODUCTION

Warts or verrucae are one of the common cutaneous viral infections, caused by human papilloma virus. They are benign tumours which commonly involve the skin and other epithelial tissues[1]. Patients seek treatment for a variety of reasons including the unsightly appearance, the pain and the discomfort it causes. The ideal aim during treatment of warts should be to remove the wart without recurrence, avoid mutilating procedures and to help the body's immune system to deal with the infection better, producing lifelong immunity against the viral infection[2].

Treatment of warts is difficult though many modalities are available, more so with multiple and recalcitrant warts. Warts may need differing treatments based on their type and site.

Cryotherapy with liquid nitrogen is a very commonly used modality of treatment for warts and is a simple, safe and inexpensive office procedure. But it requires treatment of every individual lesion and this makes treatment of multiple warts by this technique, cumbersome.

Homologous autoimplantation is a simple and novel method of treatment of warts which involves harvesting a bit of the wart tissue and implanting it subcutaneously. This, theoretically induces an immune response which leads to resolution of warts[3].

In this background, we planned to conduct a study to compare the efficacy of cryotherapy with liquid nitrogen, the commonly used modality of treatment and homologous autoimplantation of wart, a novel method of treatment for multiple warts.

# REVIEW OF LITERATURE

## HISTORY

The history of warts dates back to 400 – 370 B.C when they were well known among the Greeks and Romans. The term 'verruca' was first used by Sennertus, which meant a steep place or height appearing as little hills. Martiales first used 'condyloma' which is a greek word. Roman – Hellenistic cultures called genital warts as ficus and thymion. Celsus described 3 types of warts – achrochordon in children, thymion or genital warts and myrmecia or plantar warts[1]. The sexual transmission of genital warts was known to Romans. But until the 19$^{th}$ century they were thought to be some form of syphilis or gonorrhoea. Daniel Turner (1712) said that warts were caused by the 'nutricious juices' seeping from damaged nerve terminals. The infectious nature of warts was first described by Joseph Payne (1891) following the observation that he developed warts after treating a patient with the same. It was later in 1950 that Strauss and his co workers demonstrated the causative virus under the electron microscope. Melnick in 1992 coined the acronym PAPOVA noting the striking similarity of the wart virus with those of the polyoma virus of mice and the vacuolating virus of monkeys (SV40). Later the first detailed study of papova virus was done by Klug et al[4].

## EPIDEMIOLOGY

Warts occur worldwide and the incidence is more or less the same everywhere. Any age group can be affected but it is uncommon in infancy and old age. Peak age is between 12 and 16 years[5,6]. Plane warts are common in childhood and among females than in males, among adults. Genital warts are more common in the age group of 20 to 29 years. There is a slight male preponderance among genital warts. The estimated prevalence of anogenital warts is 1% of the sexually active population in the USA[7]. According to a study conducted by the East Anglian Branch of the Society of the Medical Officers of Health, the incidence of warts and plantar warts amongst school children in East Anglia showed no sexual predilection[5].

## INCUBATION PERIOD

The incubation period ranges from a few weeks to many months and experimental infections took 20 months to produce clinical warts[8]. A prospective study of sexual contacts of patients with genital warts indicated an incubation period of about 3 weeks to 8 months (average – 2.8 months).[9]

## HUMAN PAPILLOMA VIRUS

Human papilloma virus is a double stranded DNA virus of the papova virus family. It is a spherical virus measuring approximately

50nm in diameter. The genome of the virus, a covalently closed circle of super coiled DNA, is placed inside a non-enveloped icosahedral capsid. Detergents can open the capsid and the antigen can be exposed, as can formalin and high temperature. Its molecular weight is 5 X $16^6$ Daltons. Each genome is made of 800 nucleotide base pairs and codes for viral proteins classified as 'E' (early) and 'L'(late) proteins. The 'E' genes are required for viral replication and the 'L' genes for structural proteins that form the capsid[10].

**HPV TYPES :**

| TYPE OF WART | HPV TYPE |
|---|---|
| Plantar warts | 1, 2, 4 |
| Common warts | 2, 4, 1, 7, 57 |
| Plane warts | 3, 10, 41, 27 |
| Epidermodysplasia verruciformis | 5, 8, 9, 12, 14, 15, 17, 19-27, 36, 46, 47, 49, 50 |
| Genital warts (low risk of malignancy ) | 6, 11, 30, 34, 40, 42-44 |
| Genital warts (high risk of malignancy ) | 16, 18, 31, 33, 35, 39, 45, 51 |

**MODES OF TRANSMISSION**

The source of infection is a clinical or subclinical case of HPV infection, as well as virions which may be present in the environment. It is transmitted by contact directly or indirectly[11]. The important

predisposing factor is disruption of the epithelium, skin or mucosa. Home, school, barracks, swimming pools and instruments used by barbers and cheiropodists and shared towels provide opportunities for spread of the infection[12]. Shaving can cause spread of warts to different areas of the face. Certain occupations, in which the individuals are prone to injury and come in contact with the flesh of animals like butchers, fish and poultry workers, have high incidence of warts. Infection from the mother's genital tract at delivery appears to be the most common cause of anogenital warts in children presenting upto 2 years of age[13].

Iatrogenic transmission can occur in gynecology clinics by sharing instruments like specula, which can spread the infection from one person to another. Viral particles have also been detected in the fumes that emerge on treating warts by electrosurgery or laser which puts the operator to the risk of acquiring laryngeal warts.

Anogenital warts are usually acquired by sexual transmission. Rarely it is spread by non-sexual modes.

**INFECTIVITY**

Genital warts are the most infective type of warts. Almost two thirds of the sexual contacts of patients with genital warts develop or have subclinical warts[14]. The infectivity of other types is lower. Low risk anogenital HPV types are HPV types 6 and 11 which rarely progress to invasive disease. The high risk types are HPV types 16 and 18 and are

found in approximately 40 to 60% and 10 to 20% of all cervical carcinomas, respectively[15].

The increased incidence of warts in the recent years is probably due to the increased awareness among public and the easy availability of health care services. The recent trend showing an increase in the number of genital warts reflects the changing cultural attitude towards sex.

**PATHOGENESIS:**

Presumably exogenously acquired HPV is inoculated into the viable epidermis through breaks in the skin. Following the entry, the single viral genome becomes resident within the epithelial basal cells. As the basal cells replicate, the viral genome is duplicated and transported within the cells as they migrate upward through the differentiating epithelium. Acanthosis is due to the hyperplasia of the proliferative basal cell population and retention of the upper stratifying keratinocytes.

Once established, the infection can spread to other areas, more often due to direct inoculation than by viremia. The wart may then continue to increase in size or stabilize. It may resolve spontaneously or may continue with little change.

## PATHOLOGY

### COMMON WARTS

Hyperplasia of all the layers is seen, which includes hyperkeratosis, acanthosis and papillomatosis. Parakeratosis occurs in columns or tiers over papillomatous projections, above a focus of vacuolated cells. There is absence of granular cells above the papillomatous crests, but are increased in number in the intervening areas. The granular cells contain coarse keratohyaline granules in clumps, seen as eosinophilic inclusion bodies. Koilocytes are seen in the upper layers of the stratum malpighii especially in the granular layer, which are large vacuolated keratinocytes. Their nucleus is small and pyknotic surrounded by a perinuclear halo of clear cytoplasm. Elongated rete ridges point towards the centre of the wart (arborisation). The nuclei may be vacuolated containing viral inclusion bodies, seen as basophilic inclusions. The dermis may show a few changes like dilated capillaries in the papillomatous projections or a lymphocytic infiltrate.

In filiform warts, the papillae are more elongated than that seen in common warts.

### PALMOPLANTAR WART

The histopathology of superficial palmoplantar wart is similar to that of verruca vulgaris. Deep palmoplantar warts show numerous eosinophilic granules in the cytoplasm of many cells. They are seen in the

lower epidermis and are found to gradually enlarge in the upper stratum malpighii where they coalesce to form large irregularly shaped, homologous inclusion bodies. These surround the nucleus, which may be vacuolated or may be separated from it by perinuclear vacuolization. The stratum granulosum is usually absent. The cells of the stratum corneum are nucleated, the nuclei are rounded and deeply basophilic, surrounded by a clear zone. There is eosinophilic intracytoplasmic material which fuses with the keratin produced by the less altered cells. Some cells of the upper stratum malpighii show small round intranuclear eosinophilic inclusion bodies.

Apart from the similarities to common warts, they differ from them in being deep to the plane of the skin and extending well into the dermis. Hyperkeratosis is prominent, acanthosis is also present but papillomatosis is only mild.

**PLANE WARTS**

They resemble verruca vulgaris but the changes are less intense. It is characterized by the presence of hyperkeratosis, hypergranulosis, acanthosis and vacuolated cells in the upper stratum mapighii. Hyperkeratosis and hypergranulosis are less pronounced as compared to common warts and parakeratosis and papillomatosis are absent. Diffuse vacuolization of cells is present. Stratum corneum shows a pronounced basket weave appearance and the stratum granulosum is uniformly

thickened. On regression, the warts show superficial lymphocytic infiltrate in the dermis with exocytosis and apoptosis of cells in the epidermis.

**ANOGENITAL WARTS**

The stratum corneum shows little thickening and there is marked acanthosis with papillomatosis. Mucosal lesions show parakeratosis. The rete ridges form thick round bands extending into the vascular dermis with a well defined border. The most diagnostic histological picture is the presence of epithelial cells showing distinct perinuclear vacuolization in the granular and spinous layers, especially in the dells between knucle like papillomatosis. These vacuolated epithelial cells are larger in size and contain round hyperchromatic nuclei. Vacuolization is not as prominent in other types of warts. Since vacuolization occurs normally in the upper layers of mucosal surfaces, it is significant only if it extends into the lower portion of stratum malpighii. There is edema of the connective tissue with increased number of dilated and tortuous capillaries. Langerhan’s cells are sometimes present. Coarse keratohyaline granules and mitotic figures may occasionally be present.

**EPIDERMODYSPLASIA VERRUCIFORMIS**

The changes in the epidermis are similar to those seen in plane warts but more extensive and pronounced. The stratum corneum shows basket weave hyperkeratosis. Sometimes, the epidermis is thickened

consisting of swollen cells in the upper part. This is a specific cytopathic effect seen in various HPV types associated with epidermodysplasia verruciformis. These large cells are seen in nests in the granular and spinous layers. The nucleoplasm is clear and the cytoplasm contains keratohyaline granules of different sizes and shapes. A few dyskeratotic cells may be seen in the lower parts of the epidermis. Some nuclei appear pyknotic while some others are round and appear empty due to peripheral accumulation of chromatin. Changes of Bowen's disease or squamous cell carcinoma may ultimately supervene.

## IMMUNITY TO HPV

The course of the HPV infection is determined by the innate immune response of the host. T cell immune responses are the most important after infection with the HPV virus, while it is the humoral immunity which prevents spread to other sites and reinfection[16]. The protection acquired by infection is type specific[17]. Cell mediated immunity is the main mechanism for rejection of warts. In disorders of cell mediated immunity, the prevalence and severity of warts and occurrence of HPV related malignancy are increased[18].

## CLINICAL FEATURES

Warts can present as different morphological types depending on the HPV type, body site, environmental factors and immunity of the patient.

## COMMON WARTS (VERRUCA VULGARIS)

The HPV types causing common warts are commonly HPV types 2, 1, 4, 7 and 57[13]. They are well circumscribed, rough, firm papules ranging from 1mm to 1cm in diameter. Confluence of adjacent lesions results in larger lesions. The common sites of occurrence are the dorsa of hands and the fingers. In children, they can be seen on the knees. Warts may occur along the line of trauma and this phenomenon is called Koebner's isomorphic phenomenon.Warts are usually aymptomatic, but tenderness may be present when warts occur over sites like nailbed, palmar aspect of fingers and when there are fissures in the warts or when they are secondarily infected. When occurring around the nails, they can cause morphological changes to the nail plate. When present on the eyelids, they can cause conjunctivitis and keratitis. They may also be present on the genitalia but that constitutes only 1 to 2% of anogenital warts[13]. Majority of the warts ( 67% ) resolve spontaneously in about 2-3 years[13]. Malignant change is extremely rare but has been reported[13].

## PLANE WARTS (VERRUCA PLANA)

This type of warts are caused predominantly by HPV types 3, 10, 28 and 49[13]. They are smooth, skin coloured or pigmented papules and usually measure 1mm to 5mm. The common sites are the face, dorsa of hands and shins. The lesions are rounded or polygonal in shape. Their number can range from a few to even a hundred. Adjacent warts may

coalesce to form large lesions. Spontaneous resolution of warts, which usually occurs in one month, is accompanied by signs of inflammation such as erythema, itching and scaling[19]. Depigmented haloes may be seen around the lesions. The resolution is usually due to cell mediated immune mechanisms. Plane warts have to be differentiated from lichen planus and acrokeratosis verruciformis. But the characteristic violaceous colour of the papules, oral lesions, the typical sites of lichen planus and the symmetrical distribution of the warty papules acrally on the dorsa of the hands helps to differentiate plane warts from the other two.

**FILIFORM AND DIGITATE WARTS**

Filiform and digitate warts are common in males. They are irregularly distributed and are common over the face and neck. They show finger like projections from the horny base and are common over the face, scalp and neck. Digitate warts are seen in both sexes and are common over the scalp.

**PLANTAR WARTS**

The common HPV types causing plantar warts are HPV types 1, 2, 4, 27 and 57.

They are classified as follows:

1. Superficial ( mosaic) warts

2. Deep warts ( myrmecia – anthill ) - formed by the coalescence of several lesions.

3. Rare variants

    - Nodular form
    - Pigmented verrucous variant
    - Whitish punctuate keratotic wart

The superficial mosaic warts are caused by HPV-2 and the deep myrmecia warts are caused by HPV-1. Smaller lesions may be caused by HPV-2, 4, 27 or 57. They first appear as small, shiny, deep seated papules . Later they become sharply defined rounded lesions with a rough surface surrounded by a smooth collar of thickened horn. Repeated parring reveals bleeding points and abrupt separation between the wart tissue and the protective horny ring. Most of these lesions are beneath pressure points, usually the heel or the metatarsal heads. Mosaic warts are so described due to the appearance presented by a plaque of closely grouped small warts. They are often painless but persistent. They have to be differentiated from corn, calluses and punctuate keratoderma.

**PERIUNGUAL WARTS**

This is common with nail biting. Common warts present beneath the nail or at the nail fold, disturb nail growth.

## ANOGENITAL WARTS

These are also known as condyloma acuminata (condyloma – knucle, acuminatum – pointed) or genital warts. They are commonly caused by HPV 6 and HPV 11. Very rarely the other low risk HPV types are involved. They are usually asymptomatic but may rarely cause discomfort, bleeding or discharge[20]. They usually appear as soft, pink, elongated , rarely pedunculated or filiform growths occurring over the mucosa. The common sites are the frenulum, corona and the glans penis in men and the posterior fourchette in women, which are the sites of coital friction[14]. The other sites that may be involved are the mucosal surface of the labia majora, labia minora, cutaneous surface of the labia, perimeatal skin and the groin region.

Apart from the classical acuminate type, a flat type is also seen on the penile shaft, pubis, perianal region and the groins. Common wart like lesions may be seen on the penile shaft which could be due to autoinoculation or transmission from the sexual partner. Anogenital warts may last for a few weeks to many years. Recurrences are also common which is attributed to the persistence of the HPV DNA in the dermis. Malignant change is seen with infections due to HPV types 16, 18, 31, 33 and 51.

Anogenital warts may be associated with other sexually transmitted infections like candidiasis, trichomoniasis and other non specific infections.

Anogenital warts may appear more pigmented and verrucous in children, and may be due to child abuse. So other features of sexual abuse like bruising, hymenal tear, enlargement of vaginal introitus and thickening of the anal margins have to be looked for.

**Epidermodysplasia verruciformis :**

This was first described by Lewandowski and Lutz and is characterized by chronic extensive HPV induced warts. They are common in infants and children[21]. They commonly present as widespread lesions resembling plane warts ( caused by HPV 3 and 10 ) or reddish brown macules resembling pityriasis versicolor ( caused by HPV 5 and 8). Commonly more than one HPV type is involved. It is diagnosed by the presence of widespread and resistant warts. There is no sex predilection. Almost half the patients have a family history and an autosomal recessive inheritance is noted. An X-linked inheritance is also seen[22]. Rarely, epidermodysplasia verruciformis may be localized to one limb. Absence of effective immunity is reflected by the recurrence of EDV after treatment. It is the cell mediated immunity that is defective, specifically the natural killer cell activity[23]. EDV caused by HPV types 5, 8 and 15 are associated with malignant skin tumours [24], but are however

not prone to bacterial or other viral infections. The contributory role of ultraviolet light in the carcinogenesis is suggested by the occurrence of lesions on the sun exposed sites.

## DIAGNOSIS

In most cases, the diagnosis can be made clinically and may be confirmed by histopathological examination.The HPV virus may also exist in the latent or subclinical forms in the skin and mucosa. Subclinical disease on the mucosal surface can be demonstrated by the application of 3 to 5 % dilute acetic acid and the whitening, which is due to the coagulation of nucleoproteins and cytokeratin of the HPV infected cells, can be examined under magnification. External lesions on the skin are viewed under 6X or 10X lens and lesions over the cervix and vagina require colposcopic examination. Acetowhitening test is not specific for HPV infections and is also seen in inflammatory conditions like lichen planus, atopic dermatitis, psoriasis, dermatophytosis, intra epithelial neoplasia and irritant contact dermatitis. Biopsy and histopathological examination confirms the diagnosis. HPV infection is said to be latent when HPV DNA is present in clinically and histologically normal skin. It can be identified by DNA hybridization or polymerase chain reaction. HPV DNA is also detectable in normal mucosa adjacent to treated warts, in normal neonatal foreskin and occasionally in normal skin biopsies. For clinical or epidemiological purposes, the presence of visible cutaneous warts is the definition of the disease.

## CYTOLOGY

This is a non invasive and inexpensive procedure in the diagnosis of HPV infection and neoplasia of the anogenital region. But the disadvantage is that it can be used only in epithelial sites where exfoliated cells can be collected. Cytology is less sensitive as compared to nucleic acid hybridization and polymerase chain reaction. This can be overcome by repeated cytological staining.

## NUCLEIC ACID HYBRIDISATION

This involves the detection of HPV DNA or RNA by using complimentary nucleic acid probes. This permits direct identification of the viral genome in tissue samples and has a high degree of specificity even in the absence of clinical and histological findings. Southern blot hybridization, dot blot hybridization and in situ hybridization are a few popular nuclei acid hybridization techniques.

In polymerase chain reaction, target sequences of DNA are amplified thousands of times and this increases the sensitivity of detection of the viral DNA in tissue specimens. The disadvantage with polymerase chain reaction is the false positive results especially with contamination.

## ELECTRON MICROSCOPIC EXAMINATION

Viral particles of various types of HPV appear similar on electron microscopy. The amount of viral particles in the lesions may vary with the type of wart. Older lesions may show complete absence of viral particles on electron microscopy and hence their absence does not exclude the presence of HPV.

## DIFFERENTIAL DIAGNOSIS

### Common warts:

The skin conditions commonly mistaken for warts are, molluscum contagiosum, acrochordon, solar keratosis, lichen nitidus, lichen planus, seborrheic keratosis and squamous cell carcinoma.

### Plane warts:

Freckles and lichen planus as mistaken as plane warts

### Plantar warts:

Plantar warts are difficult to distinguish from corns, callosities and digital fibrokeratomas.

**Genital warts:**

Genital warts resemble condyloma lata, lichen planus, Bowenoid papulosis, squamous cell carcinoma, pearly penile papules, skin tags and Tyson's glands.

**TREATMENT**

The ideal therapy for warts should be effective, painless, safe and cheap. Though there are a number of treatment modalities available for warts, none is totally effective. About two third of warts undergo spontaneous resolution in about two years time [25]. Hence patients, especially children with very few lesions, should be reassured about the benign nature of the lesion and the chances of spontaneous regression.

**1. Keratolytics :**

They act by causing clinical debridement of the surface of the wart or stimulating an inflammatory response. The patient is asked to soak the feet in warm water for 30 minutes after which the surface of the wart is abraded using a wart file or pumice stone. Abrasion of the wart may stimulate an immune response. This is followed by the application of salicylic acid with lactic acid. Usually 6 to 40% of salicylic acid is used.

It is usually applied in the night and removed in the morning. The penetration of the keratolytic agent is enhanced by occlusion with an adhesive plaster. This treatment is not suitable for warts over the face or

anogenital region. Salicylic acid is usually administered in a collodion or polyacrylic base or vehicle. Response to therapy is noted between 2 to 12 weeks**.**

## 2. CYTOTOXIC AGENTS

Podophyllin, podophyllotoxin, 5-flurouracil, bleomycin etc. are a few cytotoxic agents used in the treatment of warts.

### A) Podophyllin and podophyllotoxin :

Podophyllin is a plant resin obtained from the rhizome of Podophyllum peltatum and Podophyllum emodi. Podophyllin contains many cytotoxic agents of which podophyllotoxin is the most prominent. It is much more effective in mucosal warts than cutaneous warts. They disrupt the spindle formation which is necessary for chromosome alignment during mitosis, and thus, acts as an antimitotic agent[26]. They also suppress cellular nucleoside transport. These effects produce a metaphase mitotic arrest resulting in cellular necrosis. In addition, an antiviral effect has also been demonstrated[27]. Podophyllin is used as a 10 - 25% preparation in tincture benzoin, and is administered under professional supervision. The solution is applied over the are and allowed to dry for a few minutes and washed off after 4 hours. The procedure is repeated weekly or more often.

The common side effects observed are local skin reactions like burning, redness, itching and pain. Systemic absorption may result in renal toxicity, neuropathy, hepatotoxicity, coma, granulocytopenia and thrombocytopenia. Prolonged use is said to have oncogenic potential.

It is contraindicated in pregnancy[28]. It should not be used on large or bleeding warts, as the systemic absorption may result in intra uterine death[29], vomiting, diarrhoea, liver damage, renal damage, coma, peripheral neuropathy[30], bone marrow suppression[31] and death[32].

Podophyllotoxin, is an alternate to podophyllin. It can be administered by the patient, unlike podophyllin which needs professional supervision. It is used as a 0.5% solution in alcohol. Purified podophyllotoxin has a far better safety profile than podophyllin. Its major side effect is the local reaction which is largely irritant in nature, clinically manifesting as erythema, burning, tenderness and rarely, erosion.

**B) Topical 5-flurouracil:**

This is available as 5% solution, paint and ointment and is used in the treatment of recalcitrant warts. It is used particularly in treating meatal warts. It is also available in combination with salicylic acid. Its common side effects are erythema, erosion and hyperpigmentation.

**C) Intralesional bleomycin:**

Bleomycin is a cytotoxic polypeptide which acts by inhibiting DNA synthesis. It is injected directly into the wart tissue or is implanted into the wart from the surface through a bifurcated needle or a lancet. Intralesional bleomycin administration is a very painful procedure, so prior administration of local anesthetic is necessary. It can be given as 0.25-1 mg/ml upto 3 times per day to a maximum dose of 4mg or 1000 units/ml in two injections to a maximum dose of 2000 units. The side effects are Raynaud's phenomenon, nail loss or dystrophy, urticaria and lymphangitis. It is contra indicated in pregnancy.

## 3. CANTHARIDIN[33,34]

Cantharidin is a vesicant derived from the beetle, Cantharis vesicatoria. This is a mitochondrial poison which causes changes in the cell membrane, acantholysis and blistering.

The standard therapeutic regimen involves the application of cantharidin 0.7% in collodion solution to the wart under occlusion with a piece of adhesive tape for 24 hours. When the tape is removed, a blister is seen which heals over a period of one week. Usually a single treatment is sufficient for the complete destruction of the wart. Repeated therapy may be required at times and is performed at intervals of 1 to 3 weeks. The common side effect is pain from the blister.

## 4. CAUSTIC AGENTS

The commonly used caustic agents are trichloroacetic acid, saturated dichloroacetic acid, monochloroaceticacid and silver nitrate[35]. After parring, the lesions are painted with the caustic agent till a necrotic crust forms and the procedure is repeated at weekly intervals or more, as needed. Covering it with 40% salicylic acid and an adhesive tape for 2 hours increases the efficacy.

## 5. IMMUNOTHERAPY

### A) Contact sensitisers

The drugs commonly used are DNCB ( dinitrochlorobenzene ) and DPCP ( diphencyprone ). The mechanism of action of these drugs is through the induction of a type 4 hypersensitivity reaction against the complex formed by the drug bound to a protein of viral or human origin, which in turn causes regression of warts[36].The frequency and concentration of the application must be adjusted to produce a moderate degree of pruritus, edema and erythema without excessive discomfort to the patient.

### B) Interferons

These are a family of glycoproteins with significant antiviral, immunomodulatory and immunoproliferative effects. The problem with interferon therapy is that, treatment is incomplete and results in resolution

of warts but does not cause total eradication of HPV DNA from the epithelial surface. So interferon therapy is usually combined with other ablative procedures[37].

### C) Retinoids

Systemic as well as topical retinoids are used in the treatment of warts. Topical retinoids ( 0.05% ) are useful in treating plane warts. It is applied every night till desquamation occurs.

Retinoids bind to specific cellular receptors and cause alterations in the epidermal proliferation, keratin differentiation and also cause immunomodulation. The lesions respond well to therapy but relapses are frequent, so it is used only as an adjuvant.

## 6. ANTIVIRAL DRUGS

Cidofovir is an antiviral nucleoside analogue which is used both topically and intralesionally in the treatment of plantar and anogenital warts. Topical acyclovir under occlusion may be used to treat resistant warts, but requires prolonged therapy.

Formaldehyde and glutaraldehyde have virucidal properties. They are used for warts in areas where the keratin is extremely thick, like the soles. Formalin (37% ) is administered for 15 minutes at night and then the lesion is parred. Glutaraldehyde (10%) in aqueous ethanol or in gel form can also be used.

## 7. CIMETIDINE:

Cimetidine boosts the immunity nonspecifically. It can be used in chronic warts in adults and children. It is given in the dose of 30-40mg/kg/day for a period of 3 to 4 months. It gives better results when given in combination with levamisole[38].

## 8. ZINC :

Oral zinc used in the dose of 10mg/kg/day has a mild effect on the body's immune system. There is a report from a study where zinc produced 87% cure rates but the side effects were more and the drug had to be discontinued[39].

## 9. IMIQUIMOD:

It is an immune response modifier which acts by inducing the production of cytokines, especially interferon γ and tumour necrosis factor ( TNF ) α. It is used in the treatment of genital warts and is available as 5% cream. It is administered three times a week.

## 10. SURGICAL REMOVAL[40] :

This is one of the oldest therapeutic modalities for the treatment of warts. It is used in the treatment of recalcitrant warts. The disadvantages of this method are the need for local anesthesia, the post operative pain,

the risk of secondary infection, the inconvenience caused to the patient and the scar that is produced.

## 11. ELECTROSURGERY :

This method uses alternating current to destroy wart tissue. Electrosurgical machines produce outputs with frequencies of 500,000 – 3.5 million cycles / second.

The various electrosurgical procedures are electrodessication, electrofulguration, electrocoagulation and electrosection.

In **electrofulguration**, low amperage, low penetrative current is used causing superficial damage. The electrode is held at a short distance from the tissue surface and a spark jumps from the electrode to the tissue, to destroy it.

In **electrodessication**, the tip of the electrode is kept in contact on the surface of the lesion.

Both electrofulguration and electrodessication are superficial destructive procedures because the superficial carbonization forms an insulating barrier which protects the underlying tissues. Hence they are appropriate in the treatment of superficial epidermal lesions like seborrhoeic keratoses, actinic keratoses, acrochordons, plane warts and small epidermal nevi.

**Electrocoagulation** uses a moderately dampened current in a biterminal manner. In electrocoagulation, current of higher amperage and lower voltage is used and so it penetrates deeper than in electrodessication and electrofulguration, and is more destructive. It is useful in extirpating benign and malignant tumours, selective destruction of vessels, hair, nail matrix and for securing surgical hemostasis.

In **elecrtosection**, slightly dampened current is applied to tissues in a biterminal fashion. The current used is of high amperage and low voltage.

Electrosurgical procedures are useful in treating warts resistant to cryotherapy and chemical surgery. It is avoided in lesions over the vermilion border of the lips and plantar surface, since it produces unacceptable scarring. When used for periungual warts, it can cause nail dystrophy.

The mechanism of action is the local destruction by heat which is produced as the current passes through the tissue which encounters electrical resistance.

## 12. LASER :

Carbondioxide laser has been used to treat cutaneous and mucosal warts. It is useful in treating recalcitrant periungual and plantar warts. The adverse effects are post operative pain, scarring and loss of function.

The smoke plumes that emerge are said to contain viral DNA and are a risk to the operator.

## 13. PHOTODYNAMIC THERAPY :

This procedure involves the local application of aminolevulinic acid followed by irradiation with visible light. Aminolevulinic acid is taken up by the dividing cells and metabolized to protoporphyrin. This is then photoactivated and causes damage to the cells. It has been successful in the treatment of recalcitrant warts[41].

## 14. PSYCHOTHERAPY :

Hypnosis, suggestion and charming of warts are the commonly used psychological treatment methods. It has been demonstrated that the psychological factors induced by hypnosis initiate a systemic physiological response that affects the host virus relationship and lead to the regression of warts[42].

## 15. VACCINES :

Vaccines are being tried for anogenital warts. Prophylactic vaccines, based on virus like particles (VLP) are recombinant versions of the major capsid protein (L1) of the relevant HPV types. These vaccine trials have high efficacy. A vaccine that prevents cervical cancer precursors, cervical cancer and anogenital warts caused by HPV types 6, 11, 16 and 18 has been approved by the US Food and Drug

Administration for use in girls and women between the age of 9 and 26 years[43].

Since the spontaneous clearance of warts is associated with the cellular immunity, the concept of therapeutic vaccine is being tried. The aim is the the production of a vaccine which will stimulate the production of neutralizing antibodies and a cellular immune response which will clear the viral infection. Therapeutic vaccine composed of HPV-6 L2E7 fusion protein and AS02A adjuvant was evaluated in conjunction with the conventional therapies, but it failed to show an increase in the efficacy of conventional therapies.

## 16. CRYOTHERAPY

Cryotherapy is the targeted and controlled tissue destruction by cold temperatures. It is used for a number of benign, pre-malignant and malignant conditions.

**History :**

The history of cryotherapy in dermatology dates back to 2500 BC, when the Egyptians used cold to treat injuries and inflammation. Napolean's legendary surgeon, Dominique Jean Larrey used cold to facilitate amputations during his historic retreat from Moscow[44]. Between 1845 and 1851, Dr. James Arnott of Brighton, England, described the benefits of local cold application in the treatment of a

number of conditions. Arnott used salt solutions containing crushed ice at a temperature of -18° to -24°C to freeze breast, cervical, and skin cancers[45]. He also recognized the analgesic benumbing effect of cold and recommended it to anesthetize the skin before surgery[46,47]. It was in 1889, that Campbell White, New York City physician, first used either a swab, a spray, or a brass roller device for the clinical application of liquid air (-190°C) for a variety of skin conditions like lupus erythematosus, herpes zoster, chancroid, warts, and epitheliomas[48,49]. In the 1920s, Irving and Tarunacliff used liquid nitrogen (-182.9°C) in treating lichen planus and other skin conditions. Though easily available, it was hazardous, as it was combustible[50].

It was in 1950, after the world war II, that Dr.Ray Allington introduced the clinical use of liquid nitrogen (-196°C ) for a number of skin conditions[51].

Modern cryosurgery began through the combined work of a physician, Irving Cooper and an engineer, Arnold Lee[52].

They designed the prototype cryosurgical probe following which various cryosurgical apparatuses were designed by Douglas Torre,[53] Setrag Zacarion[54], Michael Bryne and many others.

It was in 1988, that Torre, Lubritz and Kuflik wrote a book on the practical aspects of cryosurgery in dermatology[55].

**Mechanism of action :**

1. Both intra and extra cellular ice formation occurs in cryotherapy. The former causes damage to the cell membranes while the latter damages the mitochondria and endoplasmic reticulum.

2. The extracellular ice formation causes a decrease in the extracellular water level and thus an increase in the solute concentrations. This in turn results in cell membrane disruption.

3. Thermal shock.

4. Denaturation of lipoprotein complexes.

5. Formation of microthrombi results in ischemic necrosis.

6. The cell damage causes release of antigens, which results in immunological stimulation.

**Cryogens and their effective temperatures :**

| CRYOGEN | EFFECTIVE TEMPERATURE |
|---|---|
| Saltice | -20°C |
| Carbondioxide slush | -20°C |
| Fluorocarbons | -30°C |
| Carbondioxide snow | -79°C |
| Nitrous oxide | -75 °C |
| Liquid nitrogen | - 20°C ° (swab) or – 196°C (spray, probe) |

**Skin conditions responsive to cryosurgery[56,57]:**

| | |
|---|---|
| 1. Naevi | • Pigmented<br>• Epidermal |
| 2. Lentigo | • Benign |
| 3. Vascular lesions | • Telangiectasia<br>• Spider naevus<br>• Pyogenic granuloma<br>• Pseudopyogenic granuloma<br>• Kaposi's sarcoma<br>• Haemangioma, lymphangioma |
| 4. Keratotic and preneoplastic | • Viral warts<br>• Molluscum contagiosum<br>• Seborrhoeic keratosis<br>• Actinic keratosis<br>• Bowen's disease |
| 5. Carcinoma | • Basal cell carcinoma<br>• Squamous cell carcinoma<br>• Lentigo maligna |
| 6. Cysts | • Epidermal<br>• Synovial<br>• Acne<br>• Mucous cyst |

| | |
|---|---|
| 7. Leukoplakia | |
| 8. Axillary hyperhidrosis | |
| 9. Scarring | • Keloid<br>• Acne |
| 10. Sebaceous hyperplasia | |
| 11. Rhinophyma | |

**CONTRAINDICATIONS:**

1. Agammaglobulinemia
2. Cold intolerance
3. Cold urticaria
4. Cryoglobulinemia
5. Cryofibrinogenemia
6. Raynaud’s disease
7. Pyoderma gangrenosum
8. Collagen vascular and autoimmune diseases
9. Multiple myeloma
10. Patients on renal dialysis
11. Patients on concurrent immunosuppressive therapy

**PROCEDURE[58,59,60,61] :**

There are five methods of application of cryotherapy.

**1. Dipstick technique** :

This is the simplest method and is useful in treating superficial and benign lesions only. Here a cotton tipped applicator is dipped into liquid nitrogen and applied firmly on the lesion till a rim of white ice formation is noticed around the lesion.

**2. Spray technique** :

This is the most popular method. There are various methods like spot freeze, paintbrush spray method, spiral spray method or rotator spray method. In this method, liquid nitrogen is poured into the spray unit upto two inches from the brim. Then the lid is screwed tight and one has to wait for 3-4 min for the pressure to build up. For a single short freeze, no anaesthesia is required but for larger lesions requiring more freeze time, local anaesthesia may be administered. The margin of the lesion is marked including a rim of normal tissue ( 1-2mm for benign lesions, 3-5mm for premalignant lesions, 5-10mm for malignant lesions ). K-Y jelly is applied to the lesion. The screw-on spray tip is held 1 cm away from the lesion and a steady spray of liquid nitrogen is directed towards the centre of the lesion and the ice field gradually extends peripherally. The spray is adjusted such that an ice ball of a constant size for a required

period is maintained ( 5 s to 30 s ). Then the lesion is allowed to thaw slowly and completely before refreezing. Repeating the freeze-thaw cycle produces greater damage than a single freeze because the conductivity of the previously frozen skin is greater and the already impaired circulation allows greater and faster depth of cold penetration. The resolution of the firmness of the ice is checked by palpating the skin.

**3. Cryoprobe technique :**

In this method, a cryoprobe which is suitable for the lesion is selected and pre-cooled before application to the lesion. Then the tip of the probe is applied firmly to the lesion and the cooling commences following which the probe is allowed to thaw completely before removing the probe from the surface of the lesion. A repeat cycle may be done if needed.

**4. Cryoroller technique** : This method is similar to the dipstick method. The surface of the lesion is first acetonised and the stainless steel or brass cylindrical end of the roller is dipped into the cryogen contained in a polystyrene, thermacol or plastic cup. It is then rapidly rolled over the acetonised surface of the lesion. The advantages of this technique are that it spares or minimizes surface necrosis, ulceration and pigmentary changes and at the same times achieves good results.

**4. Cone spray technique** : A cone of an appropriate size is chosen to encompass the field to be treated . The cone limits the lateral spread of

the cryogen and concentrates the spray. Since there is a very rapid fall in the temperature, it is more destructive as compared to the open spray method.

**ADVANTAGES[58-63] :**

1. It is an outpatient procedure
2. Patients of all ages can be treated
3. Can be used in patients who are at poor risk for surgery or general anesthesia.
4. Multiple tumours can be treated at the same time.
5. Complications are rare.
6. Good cosmetic results.
7. Cure rates are high.
8. Can be used for lesions on previously irradiated skin.
9. Can be used for lesions on sites of poor skin mobility where excision is difficult.

**DISADVANTAGES :**

1. Discomfort during the procedure
2. Post-operative edema
3. Post-operative pigmentary changes

**COMPLICATIONS**[58-63] :

**Immediate –**

- Pain
- Headache – for lesions on the forehead, temple or scalp
- Edema – especially at sites where the skin is lax
- Haemorrhage
- Blister formation
- Pain syncope

**Delayed –**

- Haemorrhage
- Post operative infection
- Granulation tissue formation
- Pseudoepitheliomatous hyperplasia

**Prolonged complications –**

- Hyperpigmentation
- Milia
- Hypertrophic scar
- Arthralgia
- Nerve damage

## MACROSCOPIC CHANGES AFTER CRYOSURGERY[59,64]:

During and immediately after a 30-40seconds freeze, a white ice field is noticed on the lesional skin following which a violet colour appears which moves from the periphery towards the centre. Following this, the deeper structures become paler and a haemorrhagic blister forms on the surface which forms an eschar which lasts for a few days or weeks. The area contracts after 10-14 days.

## FREEZE TIMES OF SOME TYPES OF WARTS[65,66]:

| Condition | Freeze time required |
|---|---|
| Common warts | 10-15s |
| Plane or filiform warts | 5s |

# 17. HOMOLOGOUS AUTOIMPLANTATION THERAPY

Homologous autoimplantation therapy is a novel mode of treating warts, which works by inducing a good cell mediated immunity that is essential for the clearance of warts.

**PROCEDURE**[3] :

A well developed verrucous papule is chosen as the donor wart. Under strict aseptic precautions and local anaesthesia, a nick is made on the wart to the level of the subcutis using a surgical blade number 11, and a chunk of the wart tissue is removed and placed on a sterile swab. Then the donor area is tightly secured using a mircopore dressing or a band-aid plaster. The recipient area is chosen on the left forearm, approximately 2 inches below the ante cubital crease. Under strict aseptic precautions and local anaesthesia, a small nick, upto the level of the subcutis, is made in the recipient area using a surgical blade number 11, in accordance with the resting skin tension lines. A tiny pocket is created along the nick and the harvested wart tissue is placed in it. It is then tightly secured using a micropore dressing or a band-aid plaster.

The patients are advised not to wet or remove the dressing at the recipient site for the next 5 days. Systemic antibiotics are to be prescribed for a period of 5 days. The patient is reviewed after 5 days when the dressing is removed. Patients are followed up every fortnightly for the

first month, and monthly thereafter for 6 months. Resolution of warts within a period of 3 months post-procedure is considered as successful treatment.

## 18. AUTOWART INJECTION THERAPY[67]:

In this method, under local anaesthesia and aseptic conditions, 3-4mm of the wart tissue is removed using a radiocautery apparatus and kept on a sterile gauze. This bit of the tissue is then crushed with distilled water using a mortar and pestle. A fine suspension of the wart tissue is obtained and injected intra muscularly into the patient's gluteal region using a disposable syringe. Patients are followed up after one week, one month and finally after two months. Complete resolution of warts by the end of two months is considered as successful treatment.

## 19. MODIFIED AUTOIMPLANTATION THERAPY[68] :

A modification of the homologous autoimplantation therapy for multiple and recalcitrant warts has been recently tried. In this technique, instead of removing a bit of the wart tissue, the donor tissue is obtained by parring the wart, and the parred tissue is implanted in the recipient site. This avoids two wounds, both at the donor and the recipient site as in the regular autoimplantation technique, reduces the discomfort as well as the risk of infection and also hastens the time taken for the procedure.

## BASIS OF IMMUNOTHERAPY IN THE TREATMENT OF WARTS

Apart from the local immunity, systemic immunity also plays a role in the eradication of the clinical manifestations of the human papilloma virus[1]. This is evidenced by the immunological alterations occurring in a patient in whom there is spontaneous or treatment induced regression of warts[69]. In these patients, it is noticed that, viral specific antibodies are significantly increased. It is also noticed that delayed hypersensitivity reaction to HPV antigen increases in regressing warts[70]. Intradermal injection of HPV antigen also acts as a booster in the antibody response and hypersensitivity response[71]. This concept is used in the treatment of multiple warts. The various modalities of therapy for warts which act on this basis are autoimplantation therapy, autowart injection therapy and intralesional immunotherapy[3,69]. The various substances used in intralesional immunotherapy are Candida antigen, mumps antigen, trichophytin skin test antigen, tuberculin antigen, BCG vaccine and Mycobacterium w vaccine[72,73,74,75,76,77,78,79].

# AIMS AND OBJECTIVES

1. To determine the efficacy of cryotherapy with liquid nitrogen and homologous autoimplantation therapy in the treatment of multiple warts.

2. To evaluate the safety and adverse effects of the two modalities of therapy.

3. To monitor the recurrence of warts following each therapeutic modality.

# MATERIALS AND METHODS

## TRIAL DESIGN

Open labelled prospective study with the approval of ethical committee.

## STUDY POPULATION

Hundred patients with multiple warts diagnosed on clinical grounds, attending the dermatology out patient clinic of Madras Medical College, Chennai, between December 2011 and November 2012

## INCLUSION CRITERIA

1. Multiple warts > 5 in number.
2. Duration below 3 years.
3. Treatment free period of 4 weeks prior to joining this study.

## EXCLUSION CRITERIA

1. Warts other than verruca vulgaris and palmoplantar warts.
2. Pregnancy and lactation.
3. Children < 12 years of age.
4. Immunosuppressed patients.

5. H/O immunosuppressive drug intake.

6. H/O cold urticaria, cryoglobulinemia

7. Raynaud's disease

8. Collagen vascular diseases.

**WITHDRAWALS AND DROPOUTS**

Subjects were informed that they were free to drop out from the study anytime, without stating any reason and records were maintained.

**TREATMENT PROTOCOL AND METHODOLOGY**

Hundred patients with multiple warts ( > 5 in number ) were randomly selected, a treatment free period of 4 weeks was ensured and baseline evaluation done considering the inclusion and exclusion criteria, and were randomly allotted into two groups. The diagnosis was made by history and clinical features. One group was treated with homologous autoimplantation therapy and the other was treated with cryotherapy with liquid nitrogen. The patients were followed up fortnightly for a period of 3 months, and monthly thereafter for a total of 6 months, and the time taken for clearance of the lesions, any complication that arises and recurrence were observed and recorded. The disappearance of existing lesions and absence of new lesions, within a period of 3 months from the onset of therapy was considered successful treatment.

The study was approved by the Institutional Ethical Committee, Rajiv Gandhi Government General Hospital and Madras Medical College, Chennai. All patients signed a written informed consent document.

**EVALUATION AT FIRST VISIT**

During the screening period, all the patients were evaluated as follows –

1. History
2. General examination
3. Systemic examination
4. Dermatological examination
5. Investigations –
    a. Complete blood count
    b. Random blood sugar
    c. Renal function test
    d. Liver function test
    e. VDRL
    f. ELISA for HIV

## FOLLOW - UP VISITS

All the patients were followed up fortnightly for 3 months and monthly thereafter, for a total of 6 months.

## ASSESSMENT OF PARAMETERS

1. Number of patients successfully treated within 3 months of starting treatment.
2. Any complication observed.
3. Recurrence of lesions.

## DATA ANALYSIS

The data were analysed with the help of SPSS win 12 software, under the supervision of a statistician. The statistical significance was set at 0.05 level and the confidence interval at 95%.

## PROCEDURE :

## I. PROCEDURE OF AUTOIMPLANTATION[67] :

A well developed verrucous papule was chosen as the donor wart. Under strict aseptic precautions and local anaesthesia, a nick was made on the wart to the level of the subcutis using a surgical blade number 11, and a chunk of the wart tissue was removed and placed on a sterile swab. Then the donor area was tightly secured using a mircopore dressing or a

band-aid plaster. The recipient area was chosen on the left forearm, approximately 2 inches below the ante cubital crease. Under strict aseptic precautions and local anaesthesia, a small nick , upto the level of the subcutis , was made in the recipient area using a surgical blade number 11, in accordance with the resting skin tension lines. A tiny pocket was created along the nick and the harvested wart tissue was placed in it. It was then tightly secured using a micropore dressing or a band-aid plaster.

The patients were advised not to wet or remove the dressing at the recipient site for the next 5 days. Systemic antibiotics were prescribed for a period of 5 days. The patient was reviewed after 5 days when the dressing was removed. Patients were followed up every fortnightly for the first month, and monthly thereafter for 6 months. Resolution of warts within a period of 3 months post-procedure was considered as successful treatment.

## II. PROCEDURE OF CRYOTHERAPY:

In this study, the dipstick method of application of cryotherapy was followed. In this method, first the affected area was cleaned with a disinfectant. The procedure produces pain or a stinging sensation, so local anesthesia like 1% lignocaine injection or topical anesthesia was used in children or when warts are present over sites where the procedure causes excess pain. A cotton bud was dipped into the liquid nitrogen in a container and was applied firmly on the wart till a 2 to 3 mm halo of ice

was formed. The swab was chosen to be smaller than the size of the wart. Two freeze thaw cycles, each lasting 15 to 20 seconds was given. The procedure was repeated every other week, for a maximum of four treatment sessions. The patients were followed up every fortnightly during the first 2 months and monthly thereafter for a total of six months. The time taken for the resolution of warts, complications if any and any recurrence was noted. Clearance of all the warts within a period of 3 months from the onset of treatment was considered as successful treatment.

# OBSERVATIONS

## GROUP 1 – CRYOTHERAPY GROUP

### 1. AGE DISTRIBUTION IN THE CRYOTHERAPY GROUP :

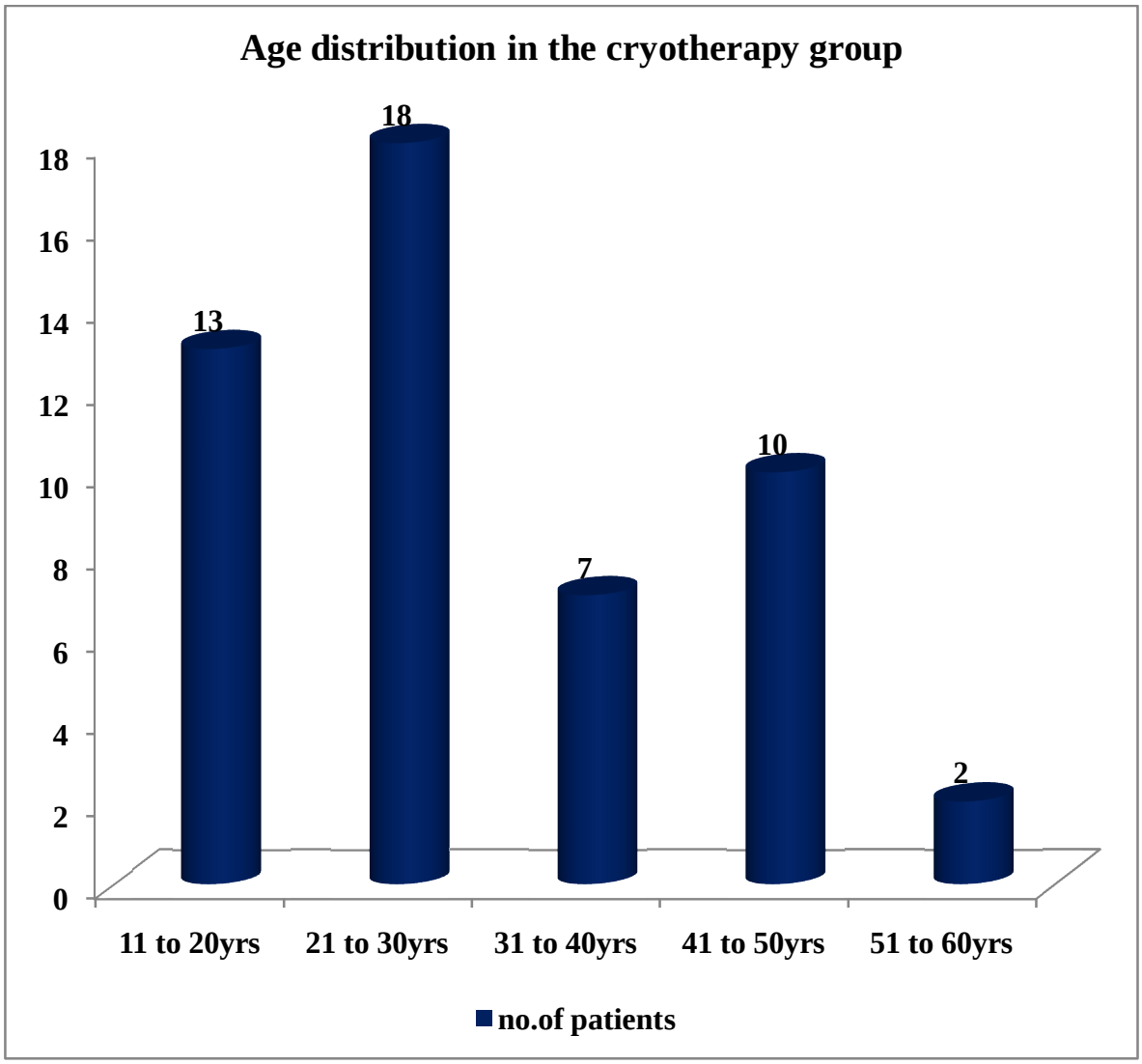
The following table ( Table 1) shows the age distribution in the cryotherapy group.

**Table 1 : Age distribution in the cryotherapy group-**

| Age group | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| 11 to 20yrs | 13 | 26.0 |
| 21 to 30yrs | 18 | 36.0 |
| 31 to 40yrs | 7 | 14.0 |
| 41 to 50yrs | 10 | 20.0 |
| 51 to 60yrs | 2 | 4.0 |

The mean age in the cryotherapy group was 29.10 years. The minimum age was 12 years and the maximum age was 57 years.

The following is the bar diagram showing the age distribution in the cryotherapy group :



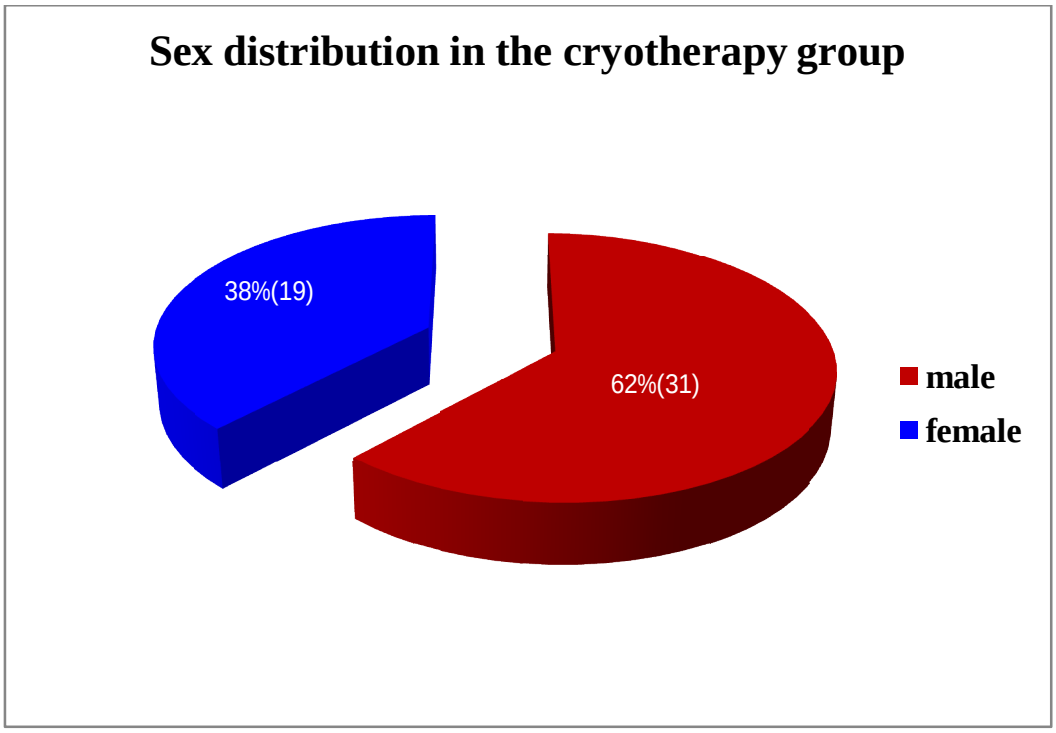
## II. SEX DISTRIBUTION :

The tabular column given below shows the sex distribution in the cryotherapy group –

**Table 2** :

**Sex Distribution in the cryotherapy group**

| Sex | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| Male | 31 | 62.0 |
| Female | 19 | 38.0 |



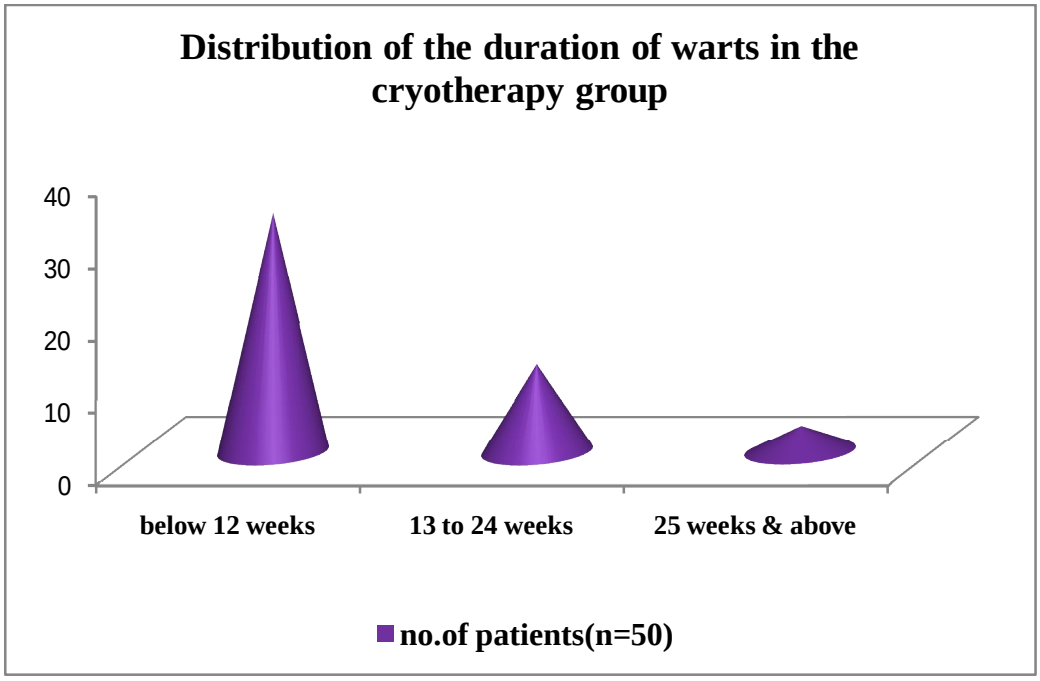
## III. DISTRIBUTION OF DURATION OF WARTS IN THE CRYOTHERAPY GROUP :

The following tabular column shows the distribution of the duration of warts in the cryotherapy group.

**Table 3 :**

**Duration of warts in the cryotherapy group**

| Duration of warts | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| Below 12weeks | 33 | 66.0 |
| 13 to 24 weeks | 12 | 24.0 |
| 25weeks & above | 5 | 10.0 |



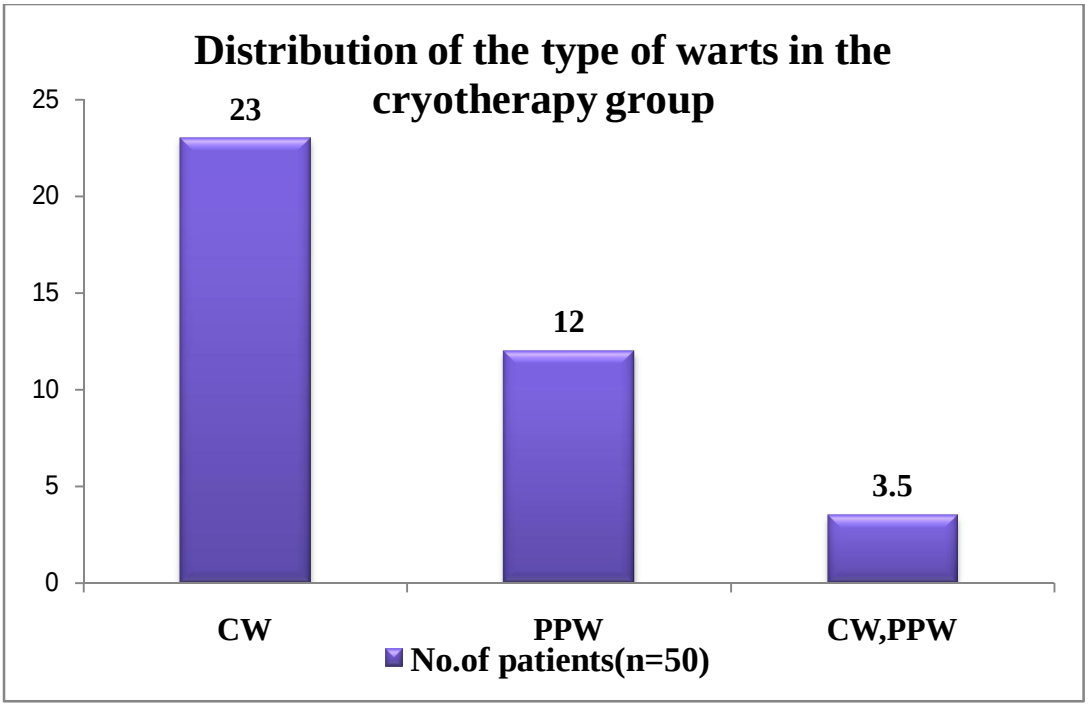
## IV. DISTRIBUTION OF THE TYPE OF WART IN THE CRYOTHERAPY GROUP :

Most of the patients in the cryotherapy group ( 23, 46% ) had common wart alone, while, 15 ( 30% ) patients had both common and palmoplantar warts and the rest ( 12, 24% ) had palmoplantar warts alone.

**Table 4 :**

**Type of wart in the cryotherapy group**

| Type of warts | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| CW | 23 | 46.0 |
| PPW | 12 | 24.0 |
| CW,PPW | 15 | 30.0 |



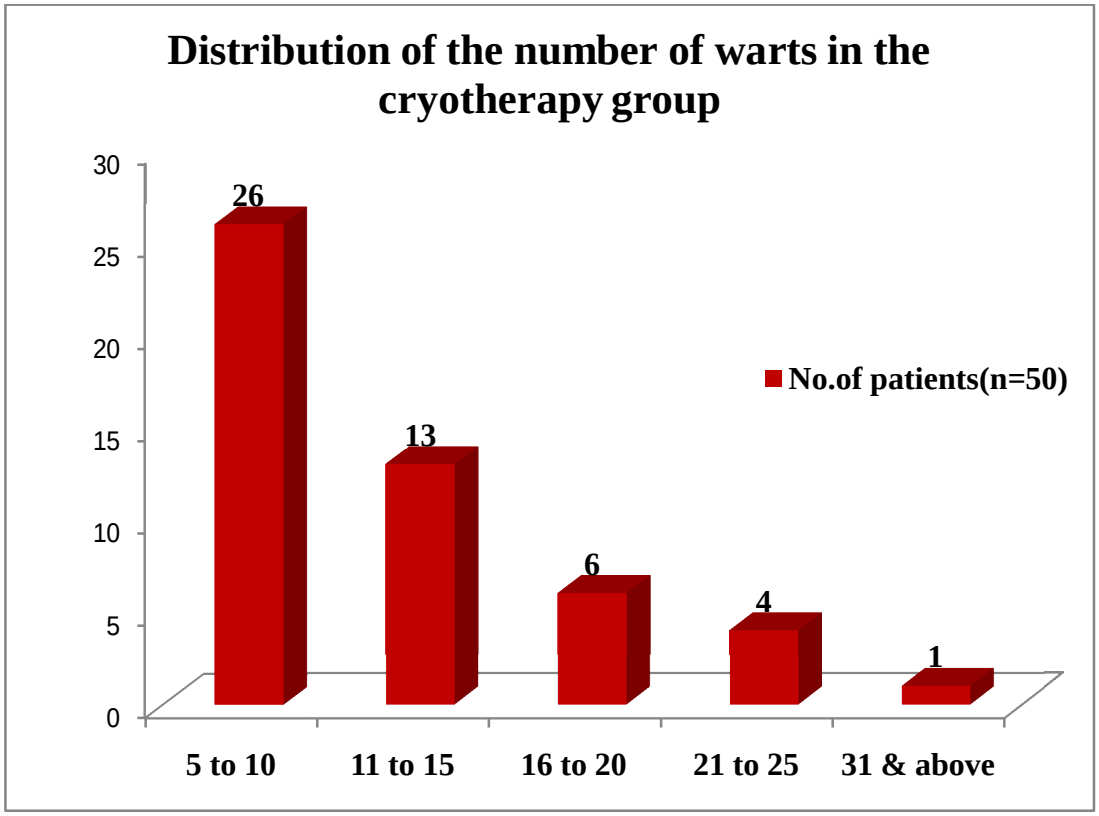
## V. DISTRIBUTION OF THE NUMBER OF WARTS IN THE CRYOTHERAPY GROUP:

The mean number of warts the patients in the cryotherapy group was 12.16, the minimum being 7 and the maximum, 31. The following table shows the distribution of the number of warts in the patients belonging to the cryotherapy group.

**Table 5 :**

**Number of warts in the cryotherapy group**

| No. of warts | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| 5 to 10 | 26 | 52.0 |
| 11 to 15 | 13 | 26.0 |
| 16 to 20 | 6 | 12.0 |
| 21 to 25 | 4 | 8.0 |
| 31 &above | 1 | 2.0 |


Distribution of the number of warts in the cryotherapy group
30
25
20
15
10
5
0
26
13
6
4
1
No.of patients(n=50)
5 to 10
11 to 15
16 to 20
21 to 25
31 & above

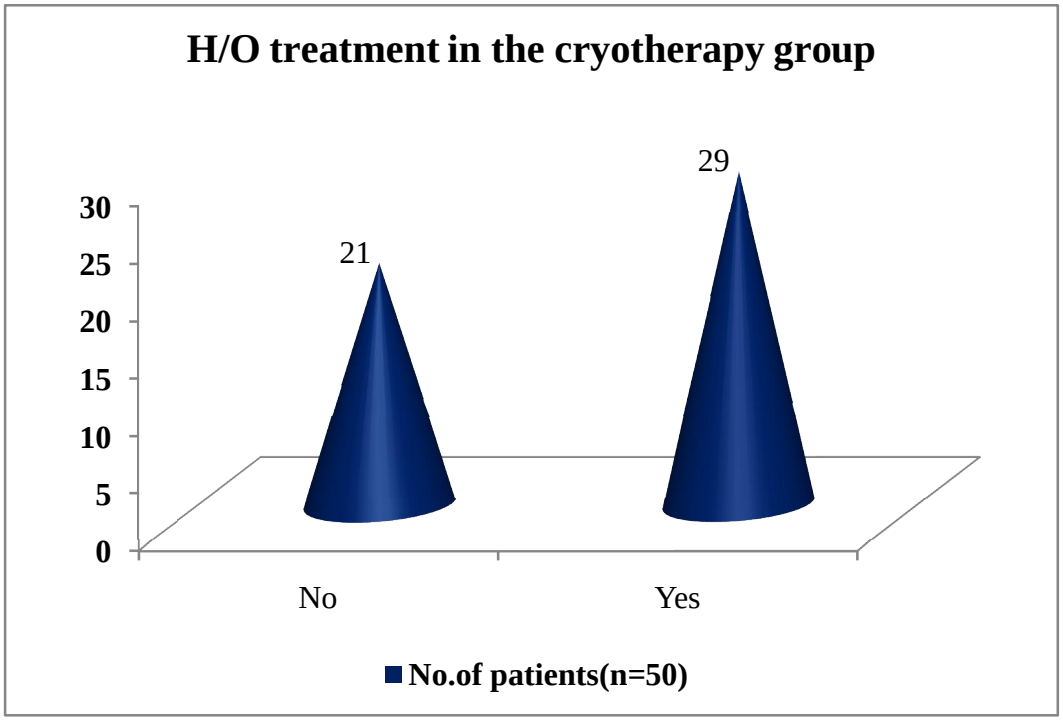
## VI. DISTRIBUTION OF PATIENTS WITH HISTORY OF TREATMENT IN THE CRYOTHERAPY GROUP

More than half of the patients ( 29, 58% ) had taken some form of treatment for warts before participating in this study. The rest had come to us anew. The following is a tabulation showing the same.

**Table 6 :**

**History of Treatment in the cryotherapy group**

| H/O Rx | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| No | 21 | 42.0 |
| Yes | 29 | 58.0 |



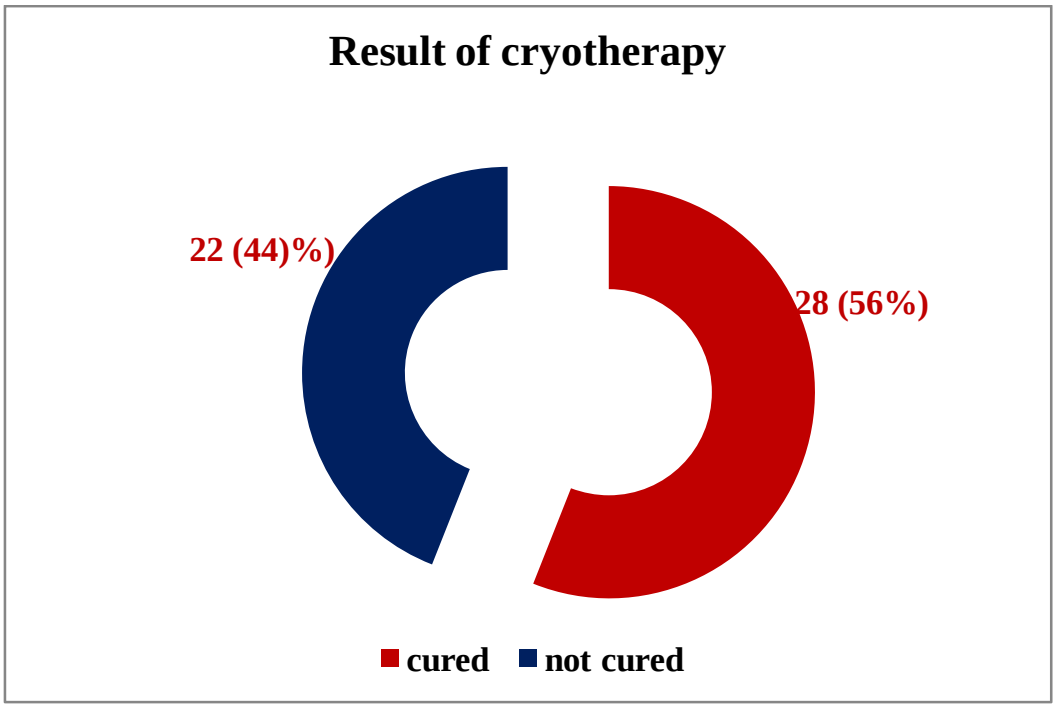
## VII. RESULTS OF THE CRYOTHERAPY

Of the 50 patients who were enrolled in the cryotherapy group, 28 (56% ) of them were cured by the end of 3 months, and the rest were not. The following table shows the result of cryotherapy at the end of the study period, followed by a pictorial representation of the same.

**Table 7 :**

**Results of the cryotherapy**

| Result | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| C | 28 | 56.0 |
| NC | 22 | 44.0 |



Before Cryotherapy

After Cryotherapy

**Before Cryotherapy**

**After Cryotherapy**

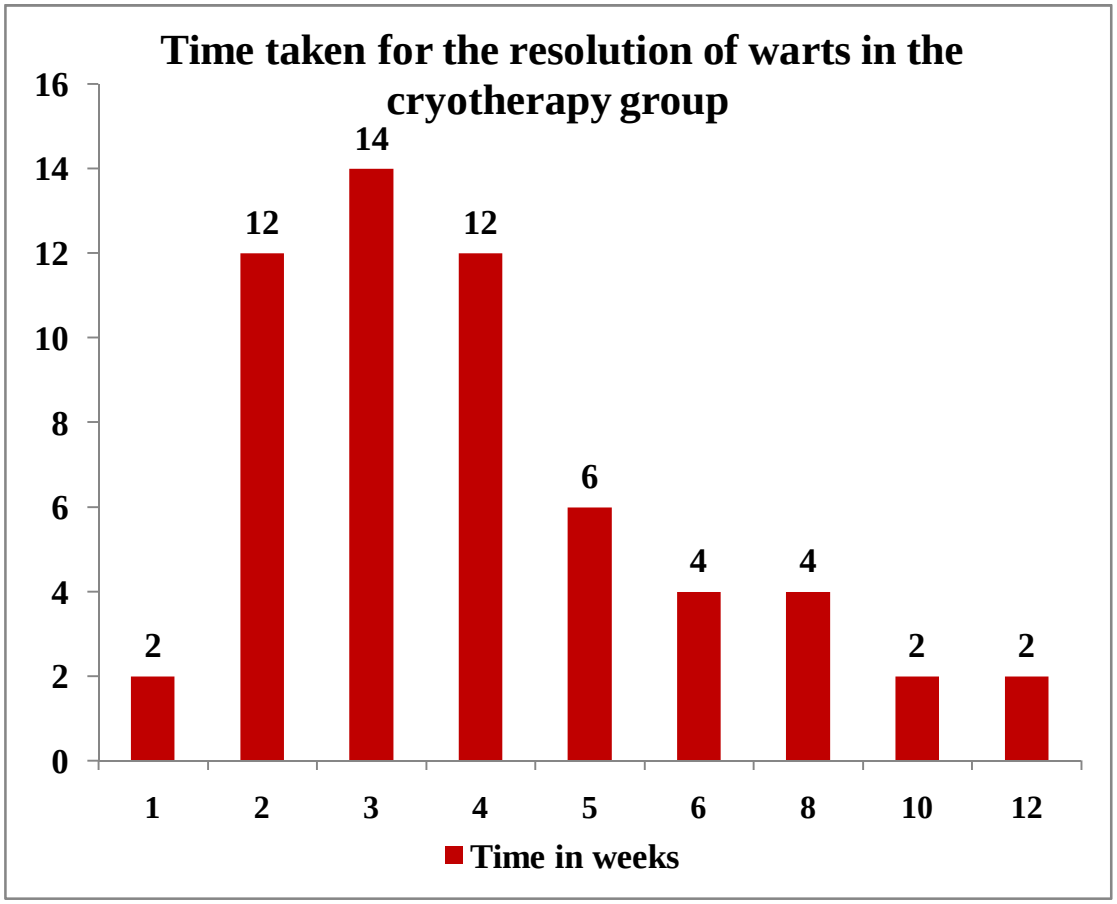
## VIII. TIME TAKEN FOR RESOLUTION IN THE CRYOTHERAPY GROUP

Most of the patients (13) were found to have resolution of warts around the 3 rd and 4th weeks after the start of therapy. The minimum and the maximum time taken were 2 and 12 weeks respectively. The mean of the time for resolution was 2.12 weeks.

**Table 8 :**

**Time taken for resolution in the cryotherapy group**

| Time taken for resolution ( in weeks ) | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| Not cured | 22 | 44.0 |
| 1 | 1 | 2.0 |
| 2 | 6 | 12.0 |
| 3 | 7 | 14.0 |
| 4 | 7 | 14.0 |
| 5 | 3 | 6.0 |
| 6 | 1 | 2.0 |
| 8 | 1 | 2.0 |
| 10 | 1 | 2.0 |
| 12 | 1 | 2.0 |


Time taken for the resolution of warts in the cryotherapy group
16
14
12
10
8
6
4
2
0
2
12
14
12
6
4
4
2
2
1
2
3
4
5
6
8
10
12
Time in weeks

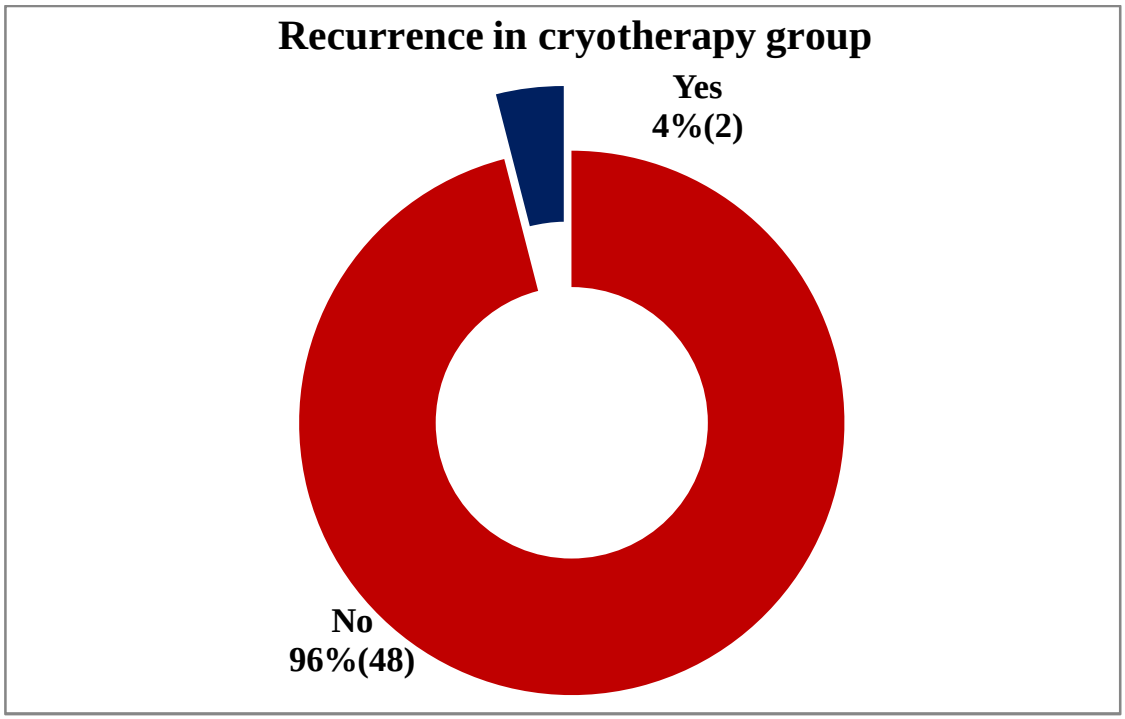
## IX. RECURRENCE OF WARTS IN THE CRYOTHERAPY GROUP

Out of the 50 patients who were given cryotherapy, 2(4%) patients had recurrence of warts. The table and the pie chart that follows show the above said data.

**Table 9 :**

**Recurrence of warts in the cryotherapy group**

| Recurrence | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| No | 48 | 96.0 |
| Yes | 2 | 4.0 |



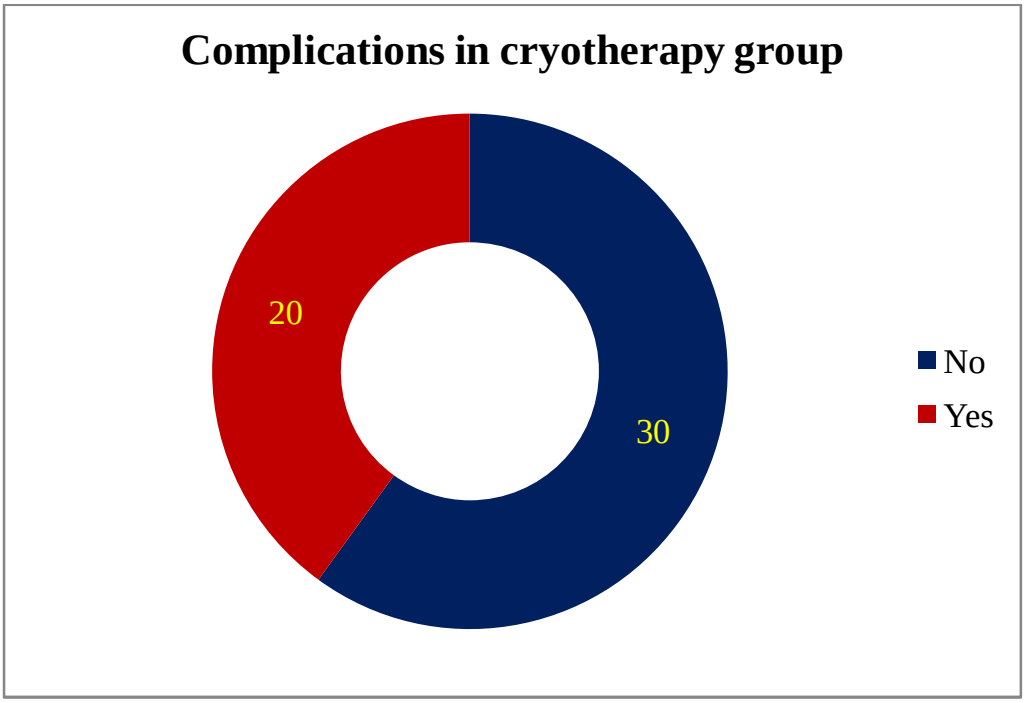
## X. COMPLICATIONS

In the cryotherapy group, 20 ( 40% ) out of the 50 patients had some kind of a complication like pain, hyperpigmentation, hypo-pigmentation, bleeding, blistering, secondary infection of the cryotherapy site and scarring.

**Table 10 :**

**Complications in the cryotherapy group**

| Complications | No. of patients (n=50) | Percentage (100%) |
|---|---|---|
| No | 30 | 60.0 |
| Yes | 20 | 40.0 |



**Blistering**

**Ulceration**

**Hyperpigmentation**

**Ulceration**

# GROUP II

# HOMOLOGOUS AUTOIMPLANTATION GROUP

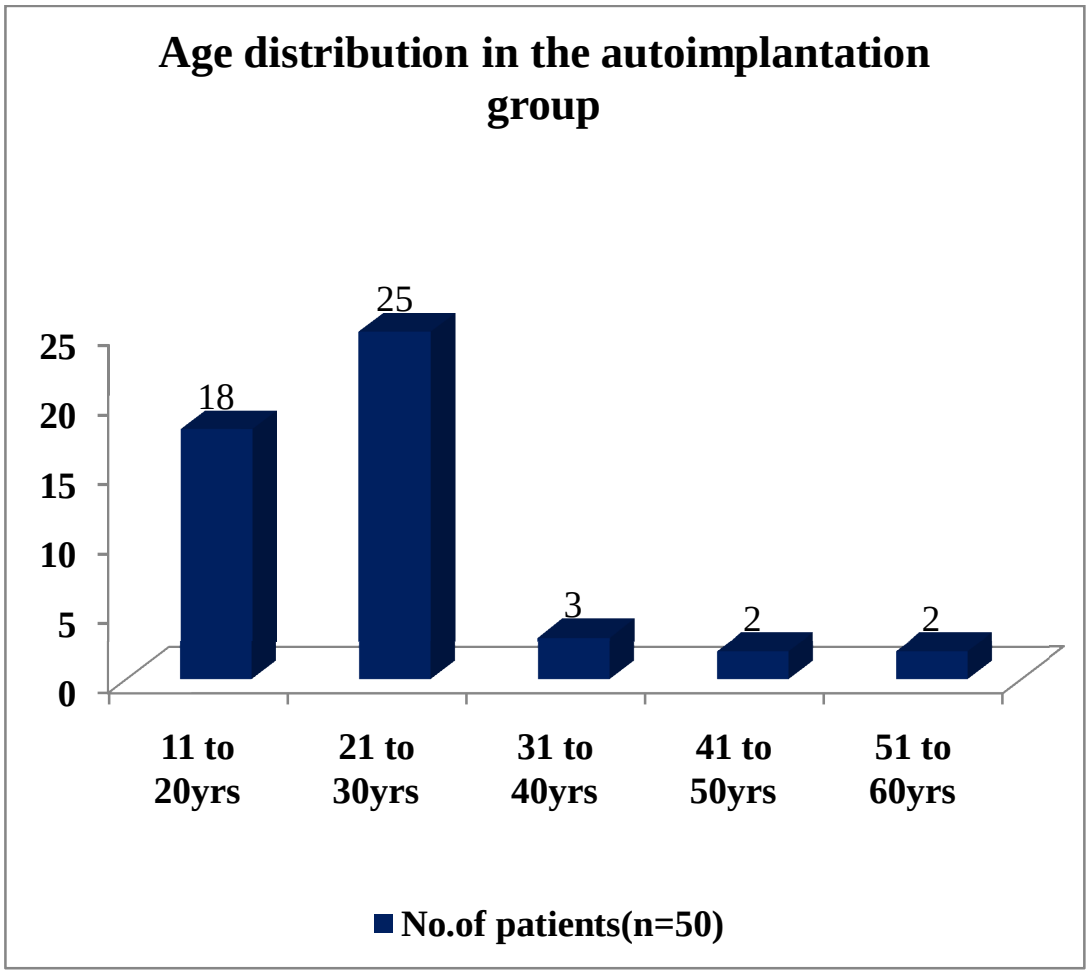
## I. AGE DISTRIBUTION IN THE AUTOIMPLANTATION GROUP

The age range of patients in the autoimplantation group was between 12 and 60 years with a mean age of 23.96. The maximum number of patients (25, 50%) were in the age group of 20 to 30 years. The following table shows the age distribution in the autoimplantation group.

**Table 11 :**

**Age Distribution in the autoimplantation group**

| Age group | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| 11 to 20yrs | 18 | 36.0 |
| 21 to 30yrs | 25 | 50.0 |
| 31 to 40yrs | 3 | 6.0 |
| 41 to 50yrs | 2 | 4.0 |
| 51 to 60yrs | 2 | 4.0 |


Age distribution in the autoimplantation group
25
20
15
10
5
0
18
25
3
2
2
11 to 20yrs
21 to 30yrs
31 to 40yrs
41 to 50yrs
51 to 60yrs
No.of patients(n=50)

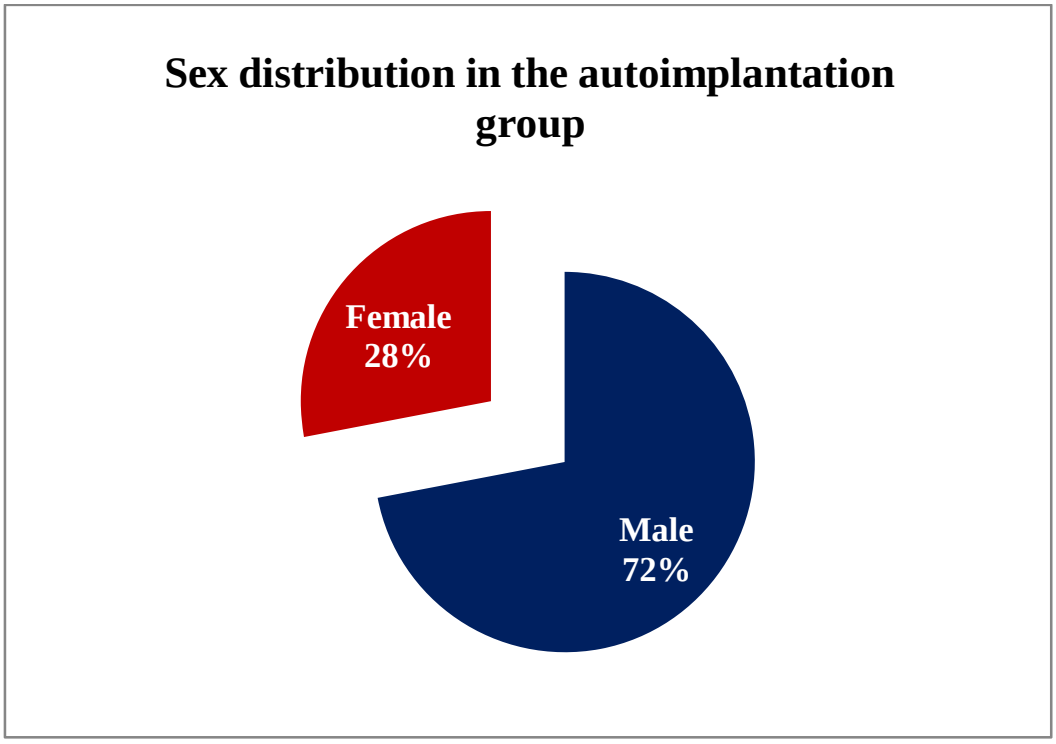
## II. SEX DISTRIBUTION IN THE AUTOIMPLANTATION GROUP

Majority of the patients ( 36, 72% ) in the autoimplantation group were males as shown in the table below and the diagram that follows it.

**Table 12 :**

**SEX DISTRIBUTION IN THE AUTOIMPLANTATION GROUP**

| Sex | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| Male | 36 | 72.0 |
| Female | 14 | 28.0 |



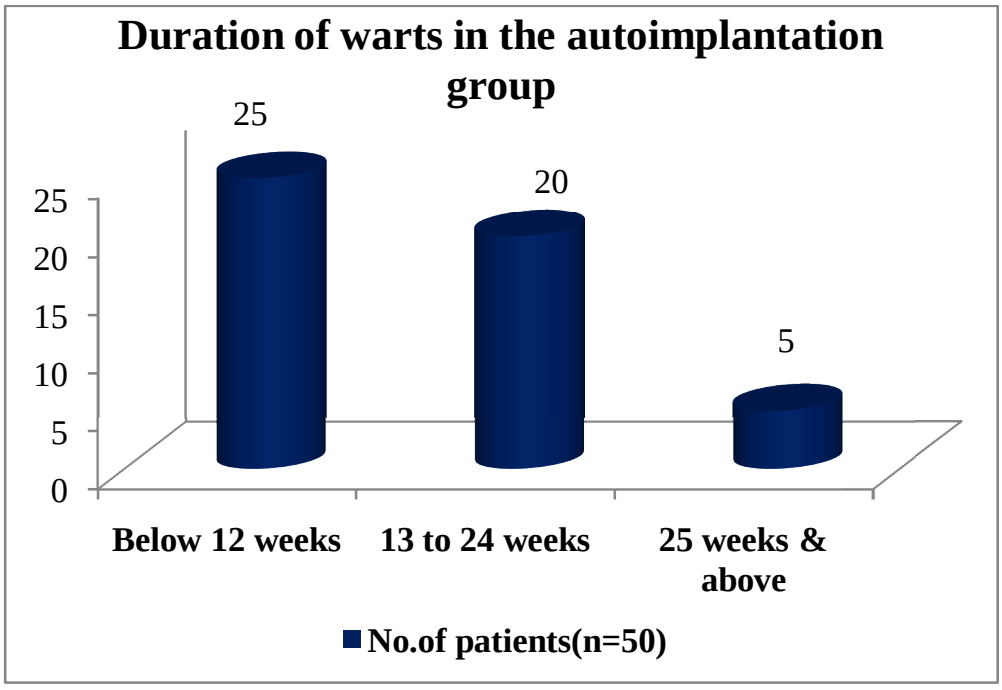
## III. DISTRIBUTION OF PATIENTS BY DURATION OF WARTS IN THE AUTOIMPLANTATION GROUP

Majority of the patients (25,50%) belonging to the autoimplantation group had warts for a period less that 12 weeks, the mean of which is 16.76. the maximum duration was 36 weeks in one patient and the minimum was 6 weeks.

**Table 13 :**

**Duration of warts in the autoimplantation group**

| Duration of warts | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| Below 12weeks | 25 | 50.0 |
| 13 to 24 weeks | 20 | 40.0 |
| 25weeks & above | 5 | 10.0 |



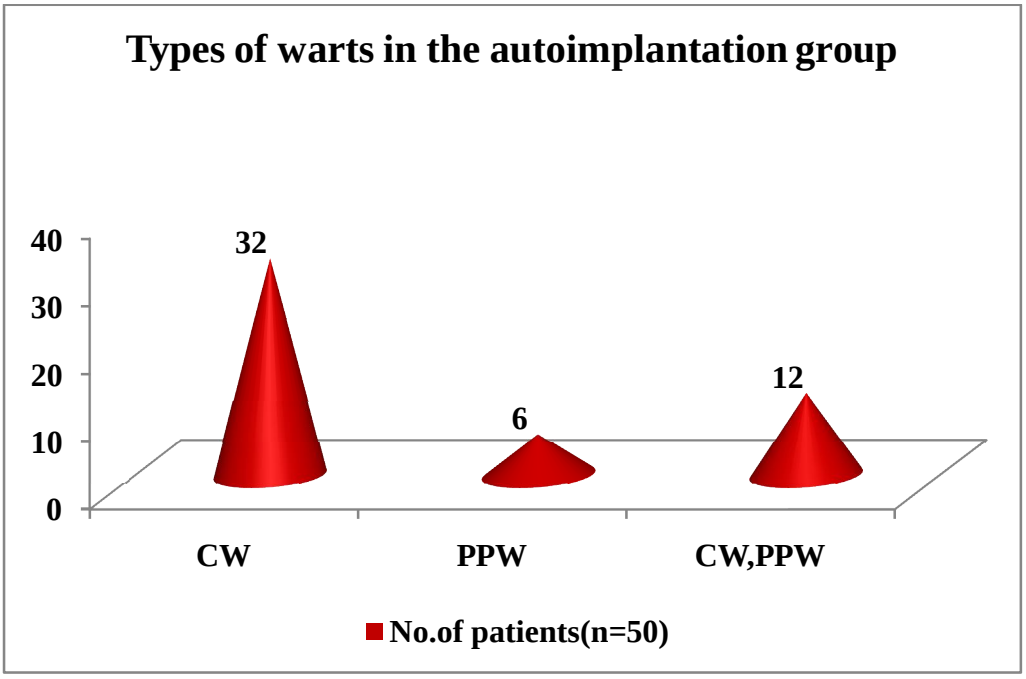
## IV. DISTRIBUTION OF THE DIFFERENT TYPES OF WARTS

Patients with common warts and palmoplantar warts were included in the study. Of the 50 patients in the autoimplantation group, 32 (64%) of them had common warts, 6 (12%) had palmoplantar warts and the rest (12,24%) had both common warts and palmoplantar warts.

**Table 14 :**

**Types of warts in the autoimplantation group**

| Type of warts | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| CW | 32 | 64.0% |
| PPW | 6 | 12.0% |
| CW,PPW | 12 | 24.0% |



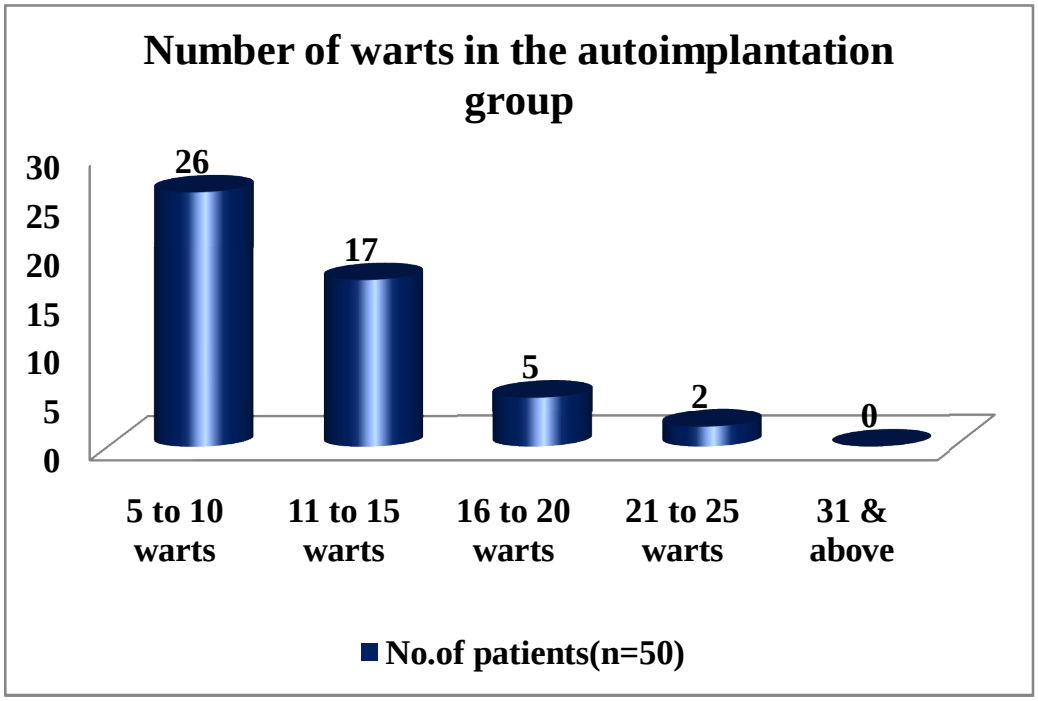
## V. DISTRIBUTION OF THE NUMBER OF WARTS IN THE AUTOIMPLANTATION GROUP

Out of the 50 patients in the study group, majority of the patients (26,52%) had between 5 to 10 warts , the mean number in the group being 11.4. The lowest number was 6 and the highest was 22.

**Table 15 :**

**Number of warts in the autoimplantation group**

| No. of warts | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| 5 to 10 | 26 | 52.0% |
| 11 to 15 | 17 | 34.0% |
| 16 to 20 | 5 | 10.0% |
| 21 to 25 | 2 | 4.0% |



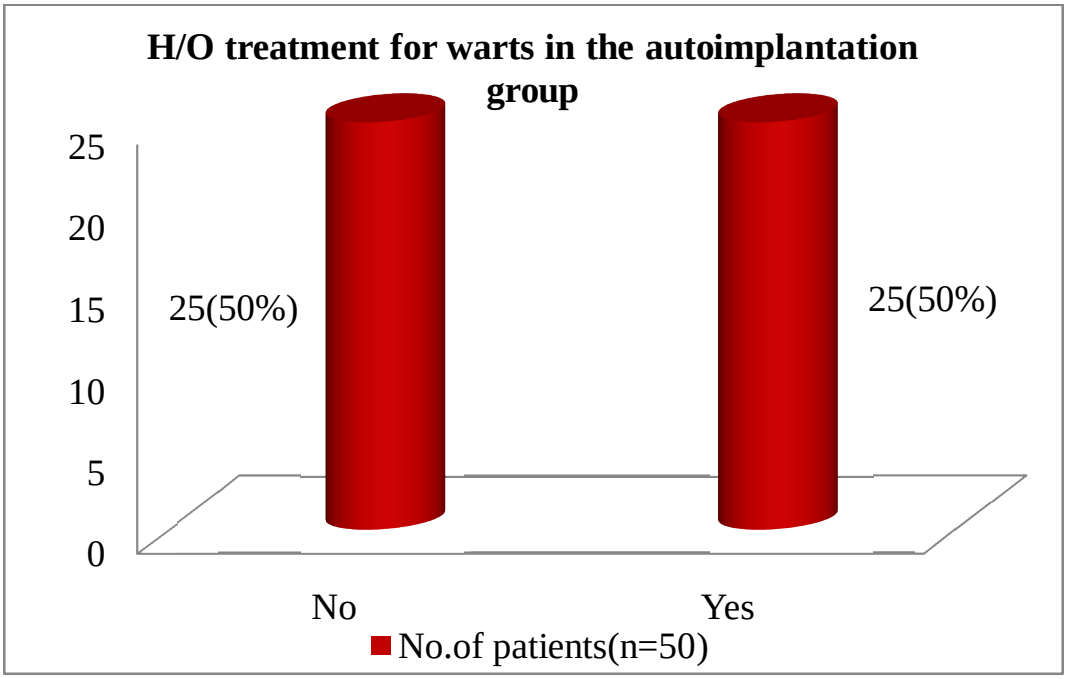
## VI. DISTRIBUTION OF PATIENTS BASED ON H/O TREATMENT TAKEN IN THE AUTOIMPLANTATION GROUP

Half (25) of the total patients had history of treatment with liquid nitrogen, electrosurgery, topical medications or native medicine. The following tabular column shows the data.

**Table 16 :**

**H/o Treatment Taken in the autoimplantation group**

| H/O Rx | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| No | 25 | 50.0% |
| Yes | 25 | 50.0% |



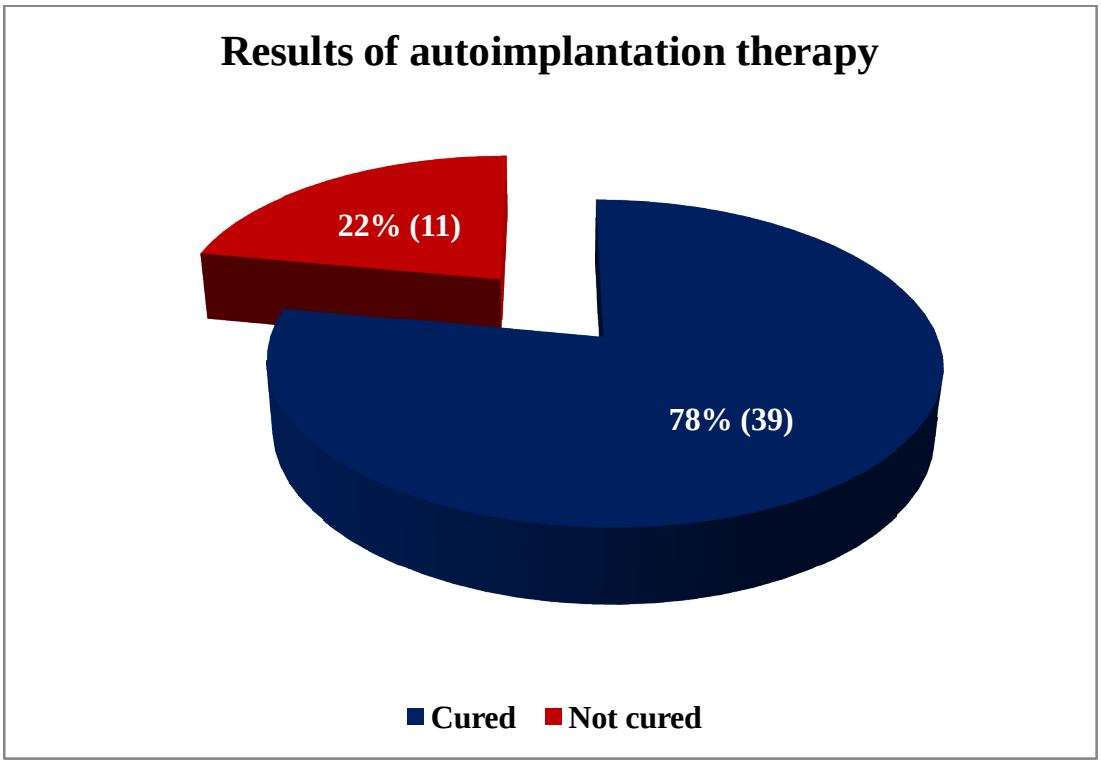
## VII. RESULTS OF HOMOLOGOUS AUTOIMPLANTATION

Out of the 50 patients, 39 (78%) of them had resolution of their lesions by the end of 12 weeks.

**Table 17 :**

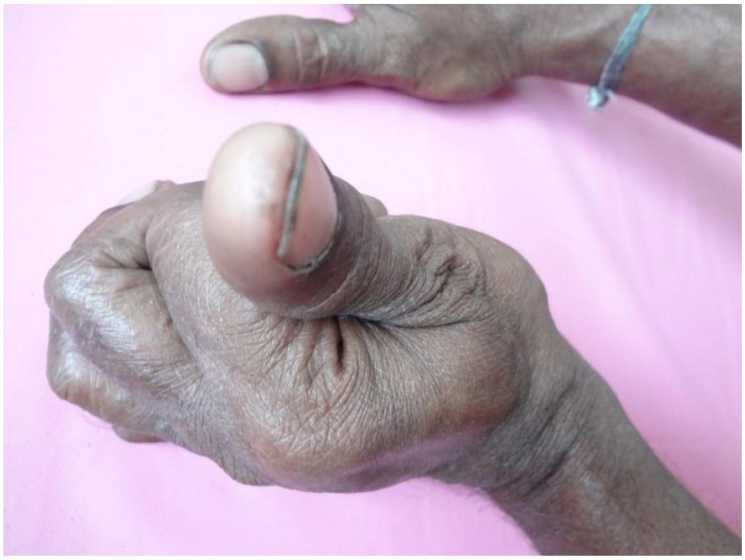
**Results of Homologous Autoimplantation**

| Result | No.of patients (n=50) | Percentage (100%) |
|---|---|---|
| C | 39 | 78.0% |
| NC | 11 | 22.0% |



## AUTO IMPLANTATION

**Before**



**4 Weeks Later**

**6 Weeks Later**

## AUTO IMPLANTATION

**Before**

**6 Weeks Later**

**8 Weeks Later**

# AUTO IMPLANTATION

**Before**

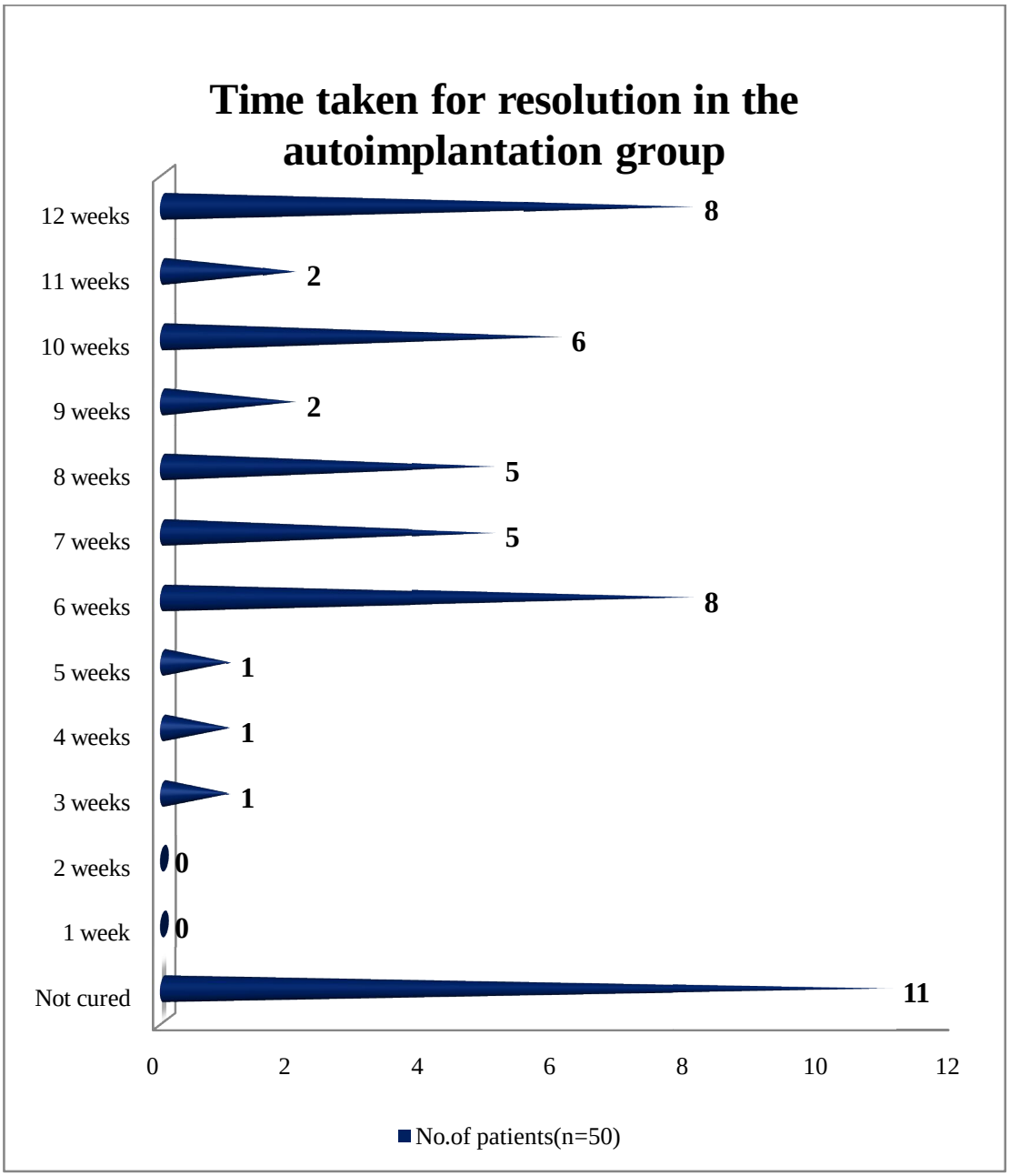
**After**

## VII. TIME TAKEN FOR THE RESOLUTION OF WARTS IN THE AUTOIMPLANTATION GROUP

The earliest response to therapy in the autoimplantation group was seen at 3 weeks and the longest time taken for resolution was 12 weeks. Maximum number of patients had their lesions resolved at 6 and 12 weeks in our study. The following table shows the above said data.

**Table 18 :**
**Time Taken For The Resolution Of Warts in the autoimplantation group**

| Time taken for resolution ( in weeks ) | No. of patients (n=50) | Percentage (100%) |
|---|---|---|
| Not cured | 11 | 22.0 |
| 3 | 1 | 2.0 |
| 4 | 1 | 2.0 |
| 5 | 1 | 2.0 |
| 6 | 8 | 16.0 |
| 7 | 5 | 10.0 |
| 8 | 5 | 10.0 |
| 9 | 2 | 4.0 |
| 10 | 6 | 12.0 |
| 11 | 2 | 4.0 |
| 12 | 8 | 16.0 |


Time taken for resolution in the autoimplantation group
12 weeks
11 weeks
10 weeks
9 weeks
8 weeks
7 weeks
6 weeks
5 weeks
4 weeks
3 weeks
2 weeks
1 week
Not cured
8
2
6
2
5
5
8
1
1
1
0
0
11
0
2
4
6
8
10
12
No.of patients(n=50)

## VIII. RECURRENCE OF WARTS IN AUTOIMPLANTATION GROUP

In the autoimplantation group, none out of the 50 patients were found to have recurrence of warts by the end of the 6 month follow up period.

**Table 19 :**

**Recurrence of warts in the autoimplantation group**

| Recurrence | No. of patients (n=50) | Percentage (100%) |
|---|---|---|
| No | 50 | 100.0% |
| Yes | 0 | 0.0% |

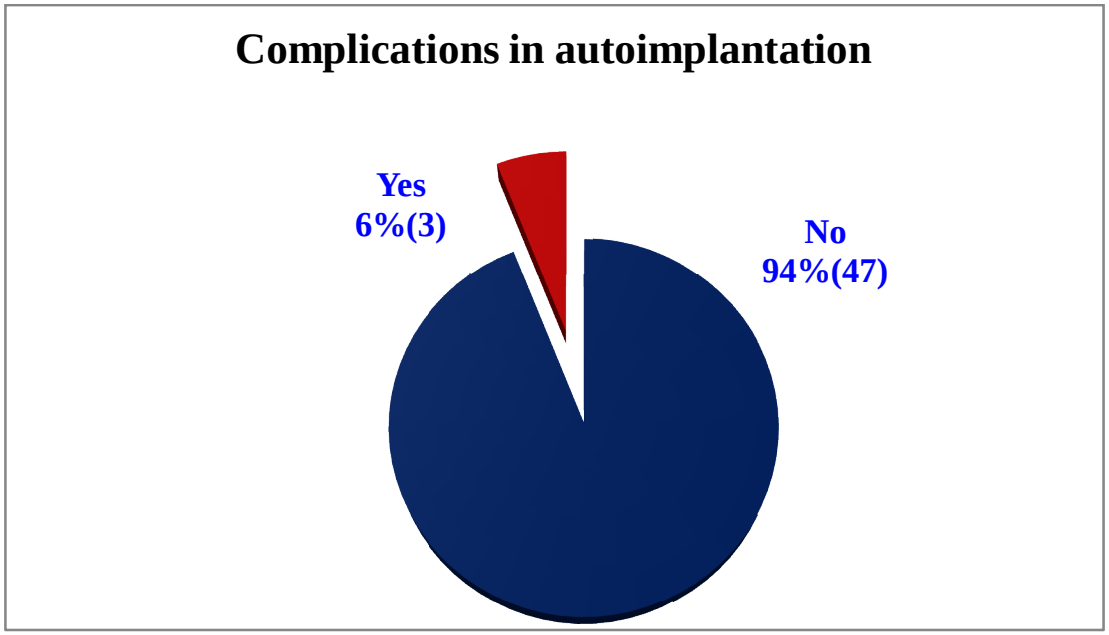
## IX. COMPLICATIONS OBSERVED IN AUTOIMPLANTATION GROUP

In the autoimplantation group, only 3 (6%) had complications of the treatment. One person had a secondary infection at the autoimplantation site and 2 (4%) patients developed an inflammatory nodule at the site of implantation of the wart. A few patients had transient hypopigmentation which disappeared in 2 weeks.

**Table 20 :**

**Complications in the autoimplantation group**

| Complications | No. of patients (n=50) | Percentage (100%) |
|---|---|---|
| No | 47 | 94.0% |
| Yes | 3 | 6.0% |



**Hypopigmentation**

## COMPARISON OF THE TWO STUDY GROUPS - CRYOTHERAPY WITH LIQUID NITROGEN AND HOMOLOGOUS AUTOIMPLANTATION

No statistical differences were noted between the two study groups in terms of age, sex, duration of wart, types of wart or H/O treatment for warts. The following table compares the mean age, sex ratio, duration of warts, number of warts and number of patients with H/O treatment for warts in the two groups.

**Table 21 :**

| | | **Cryotherapy** | **Autoimplantation** |
|---|---|---|---|
| 1. | Age (Mean in yrs.) | 29.10 | 23.96 |
| 2. | Duration (wks.) | 14.88 | 16.76 |
| 3. | Sex ratio (M:F) | 31:19 | 36:14 |
| 4. | Number of warts | 12.16 | 11.40 |
| 5. | H/O treatment | 29 | 25 |

**COMPARISON OF RESULTS OF THERAPY :**

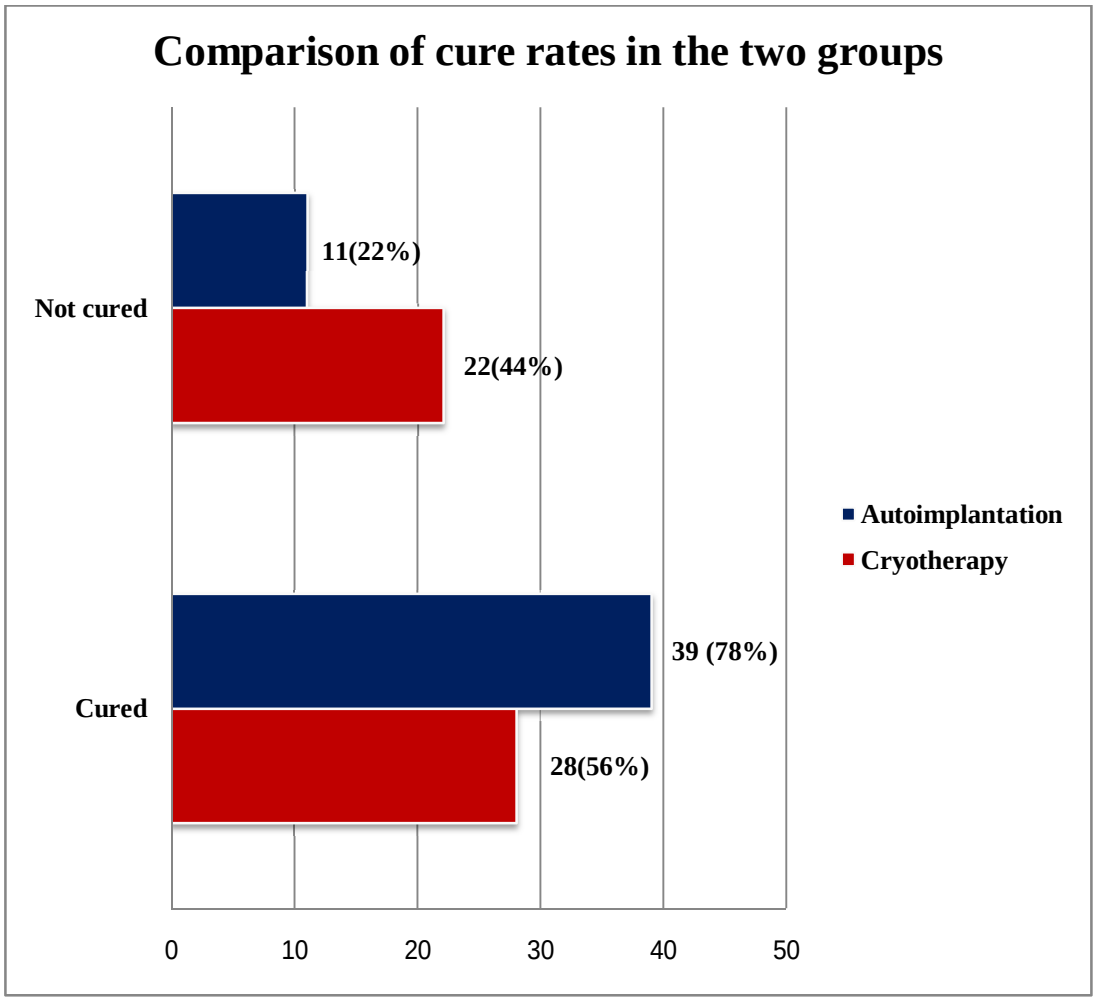
In this study, it was observed that homologous autoimplantation gave a higher cure rate (78%) as compared to cryotherapy with liquid nitrogen (56%) with a p value of 0.19 < 0.05 which is statistically significant.

The following table shows the percentage of successful therapy in the two groups :

**Table 22 :**

**Comparison of results of therapy**

| **Result of therapy** | **Samples** | | | | | | **Statistical inference** |
|---|---|---|---|---|---|---|---|
| | **Cryotherapy** | | **Autoimplantation** | | **Total** | | |
| | **(n=50)** | **(100%)** | **(n=50)** | **(100%)** | **(n=100)** | **(100%)** | |
| Cured | 28 | 56.0% | 39 | 78.0% | 67 | 67.0% | P value .019<0.05 Significant |
| Not cured | 22 | 44.0% | 11 | 22.0% | 33 | 33.0% | |


Comparison of cure rates in the two groups
Not cured
Cured
11(22%)
22(44%)
39 (78%)
28(56%)
0
10
20
30
40
50
Autoimplantation
Cryotherapy

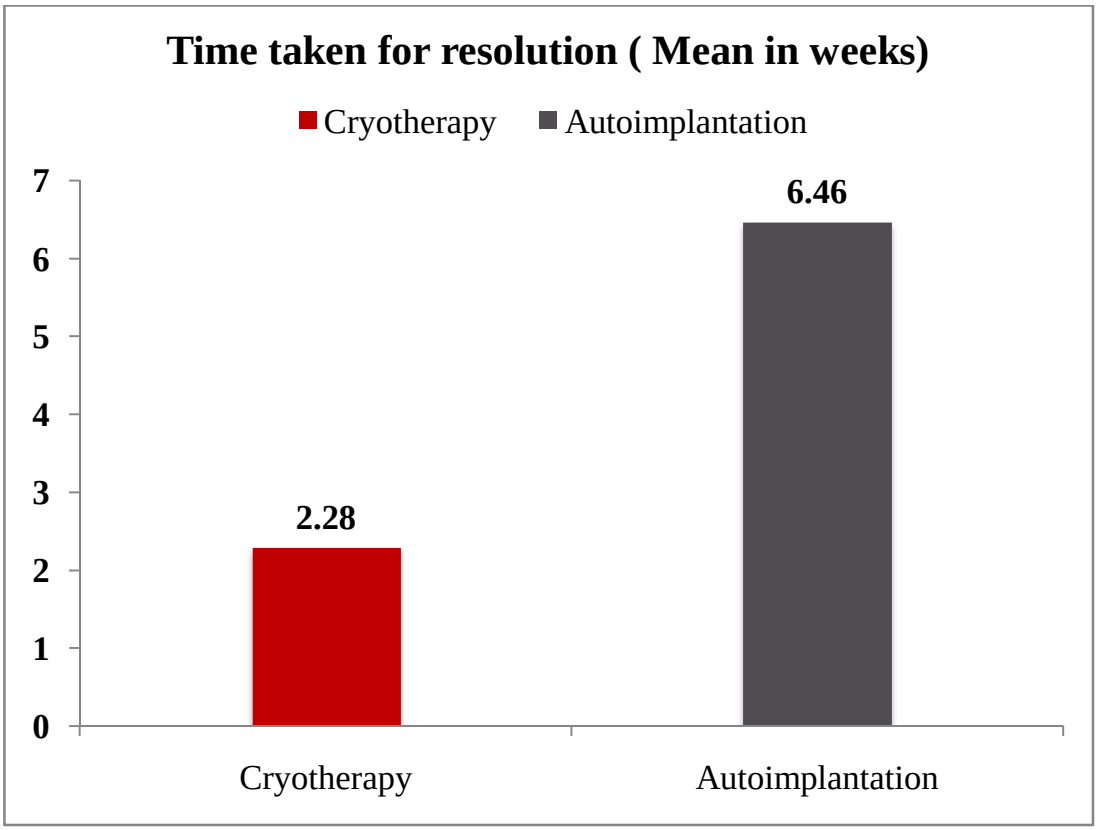
## COMPARISON OF TIME TAKEN FOR THE RESOLUTION OF WARTS

On comparison of the mean of the time taken for the resolution of warts, it was found that for the cryotherapy group, it was 2.28 weeks whereas for the autoimplantation group it was 6.46 which is statistically significant ( p = 0.002 ). So, though the cure rate was higher in the autoimplantation group, the time taken for resolution is significantly later when compared to the cryotherapy group.

**Table 23 :**

**Comparison Of Time Taken For Resolution**

| **Study group** | **Time taken for resolution (mean in weeks)** | **Statistical inference** |
|---|---|---|
| Cryotherapy | 2.28 | p value 0.002 < 0.05 Significant |
| Autoimplantation | 6.46 | |


Time taken for resolution ( Mean in weeks)
Cryotherapy
Autoimplantation
7
6
5
4
3
2
1
0
2.28
6.46
Cryotherapy
Autoimplantation

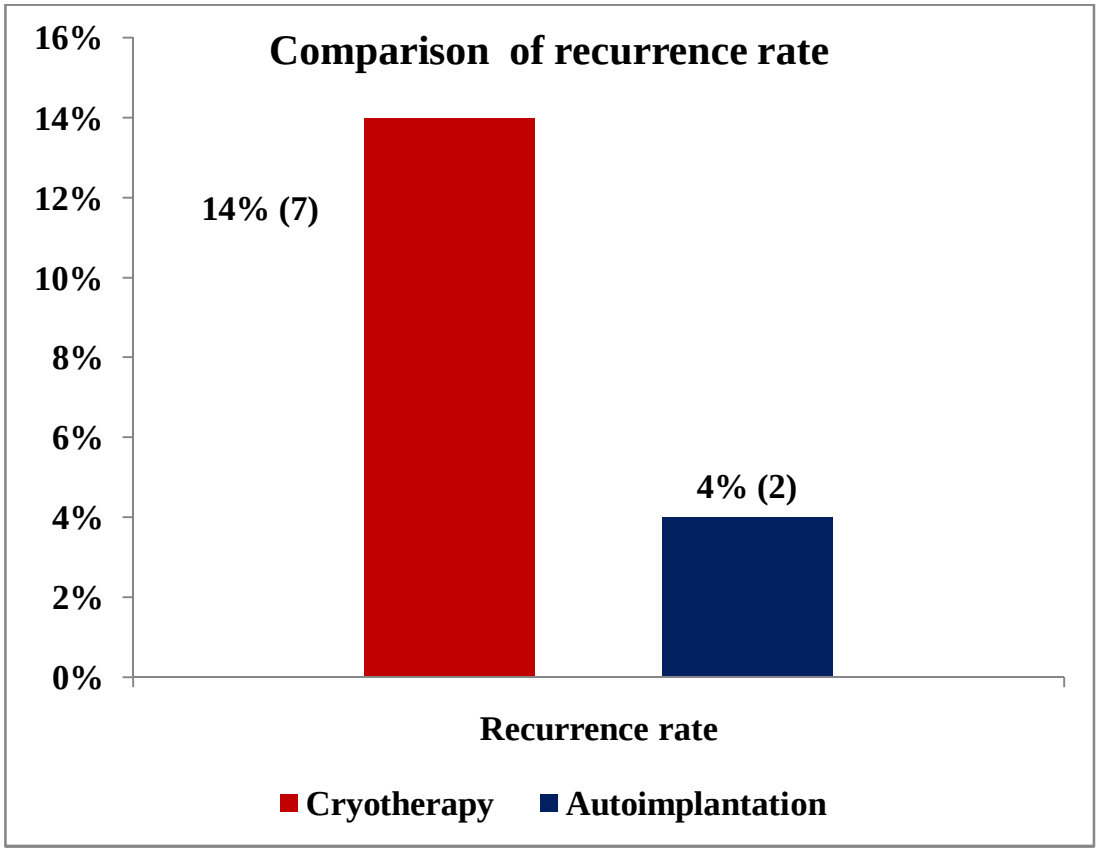
## COMPARISON OF RECURRENCE RATES

The recurrence rate was 4% (2) in the cryotherapy group whereas in the autoimplantation group, there was no recurrence. Thus the recurrence rate was found to be significantly lower in the autpoimplantation group ($p = 0.0153<0.05$).

**Table 24 :**

**Comparison of recurrence rate**

| **Recurrence** | **Samples** | | | | | | **Statistical inference** |
|---|---|---|---|---|---|---|---|
| | **Cryotherapy** | | **Autoimplantation** | | **Total** | | |
| | **(n=50)** | **(100%)** | **(n=50)** | **(100%)** | **(n=100)** | **(100%)** | |
| No | 48 | 96.0% | 50 | 100.0% | 98 | 98.0% | p value 0.153>0.05 Not significant |
| Yes | 2 | 4.0% | 0 | 0.0% | 2 | 2.0% | |


Comparison of recurrence rate
16%
14%
12%
10%
8%
6%
4%
2%
0%
14% (7)
4% (2)
Recurrence rate
Cryotherapy
Autoimplantation

**COMPARISON OF COMPLICATION RATES :**

It was found that the complication rate was much higher in the cryotherapy group (20, 40%) as compared to the autoimplantation group (3,6%). The common complications in the cryotherapy group were pain during and after the procedure, blistering, bleeding, hypopigmentation, hyperpigmentation, scarring and secondary infection. In the autoimplantation group, one patient had secondary infection at the autoimplantation site, and 2 patients developed an inflammatory nodule at the site of implantation of the wart. A few patients had transient hypopigmentation which disappeared in 2 weeks.

**Table 25 :**

**Comparison of complication rates**

| **Study group** | **No. of patients with complication** | **Statistical inference** |
|---|---|---|
| Cryotherapy | 20 (40%) | P value<br>0.002 < 0.05<br>Significant |
| Autoimplantation | 3 (6%) | |

# DISCUSSION

Warts or verrucae are a common skin condition which bother the patients by their unsightly appearance and by causing pain and discomfort[1]. There are a number of therapeutic modalities for warts but none is found to be 100% effective[2]. In our study we compared the treatment of multiple warts with cryotherapy with liquid nitrogen and homologous autoimplantation therapy.

## I. AGE :

The mean age in the cryotherapy group was 29.10 years. The minimum age was 12 years and the maximum age was 57 years. The age range of patients in the autoimplantation group was between 12 and 60 years with a mean age of 23.96. This is comparable to the age range of patients in a similar study done by P.K.Srivastava and A.K.Bajaj on autowart injection therapy for recalcitrant warts, where the age range was 10 to 57 years[3]. The maximum number of patients (25, 50%) were in the age group of 20 to 30 years.

## II. SEX :

In both the groups, males constituted majority of the study population, comparable to a study done by P.K.Srivastava and A.K.Bajaj on autowart injection therapy for recalcitrant warts, a procedure which also works by the same mechanism[3]. In the cryotherapy and the

autoimplantation groups, the sex ratio was (M:F ) 31:19 and 36:14 respectively.

## II. DURATION OF WARTS

Most of the patients in this study had warts for a duration of less than 12 weeks, with a mean duration of 15.32 weeks. Only 10% of the patients had warts for more than 6 months. This is in contrast to a similar study on autoimplantation of warts, done by V.Shivakumar, R.Okade and V.Rajkumar and the study done by P.K.Srivastava and A.K.B ajaj on auto wart injection therapy, where majority of the participants in the study had warts for more than 6 months[3,67].

## III. TYPE OF WARTS :

As in a similar study conducted by V.Shivakumar on autoimplantation therapy, we also included only verruca vulgaris and palmoplantar warts[3]. In their study, out of the 60 patients they had enrolled, 40 had verruca vulgaris and 20 had palmoplantar warts which is comparable to ours.

## IV. NUMBER OF WARTS

One of the inclusion criteria was number of warts more than 5. So all our patients had multiple warts. The mean number in the cryotherapy and the autoimplantation groups were 12.16 and 11.40 respectively, which was not statistically comparable ($p = 0.430 > 0.05$).

## V. HISTORY OF TREATMENT :

Since all our patients had multiple warts for over a period of around 3 months, almost half of our patients had tried some kind of therapy, either with topical keratolytics, electrosurgical modalities , cryotherapy or native medicines. Such patients formed 58% and 50% of the cryotherapy group and the autoimplantation group respectively, with no significant statistical difference in these terms ($p = 0.422 > 0.05$).

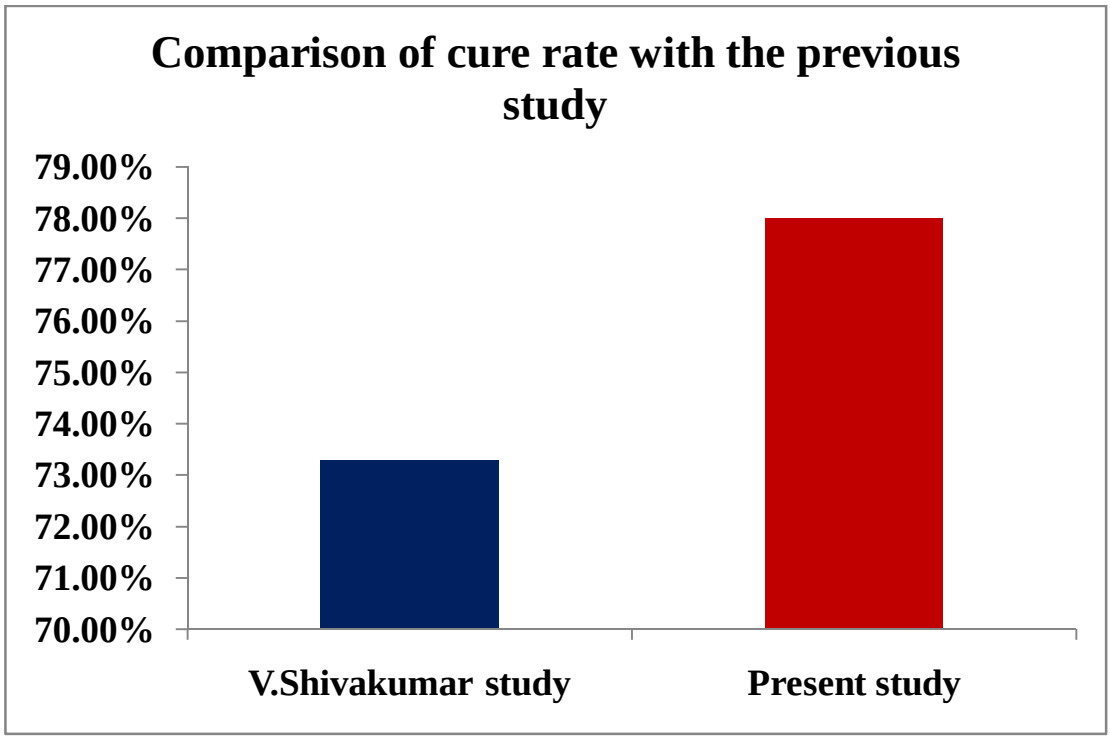
## VI. RESULTS OF THERAPY :

Our study compared the results of cryotherapy with liquid nitrogen and homologous autoimplantation therapy for multiple warts. The cure rate in the former group was 56% while that of the latter group was as high as 78%. This correlates with the cure rate observed in the study on autoimplantatio therapy by V.Shivakumar which was a little lower (73.3% )[3].

**Table : 26**

**Comparison of cure rate with the previous study**

| S.No | Study | Cure rate |
|---|---|---|
| 1. | V.Shivakumar study | 73.3% |
| 2. | Present study | 78% |

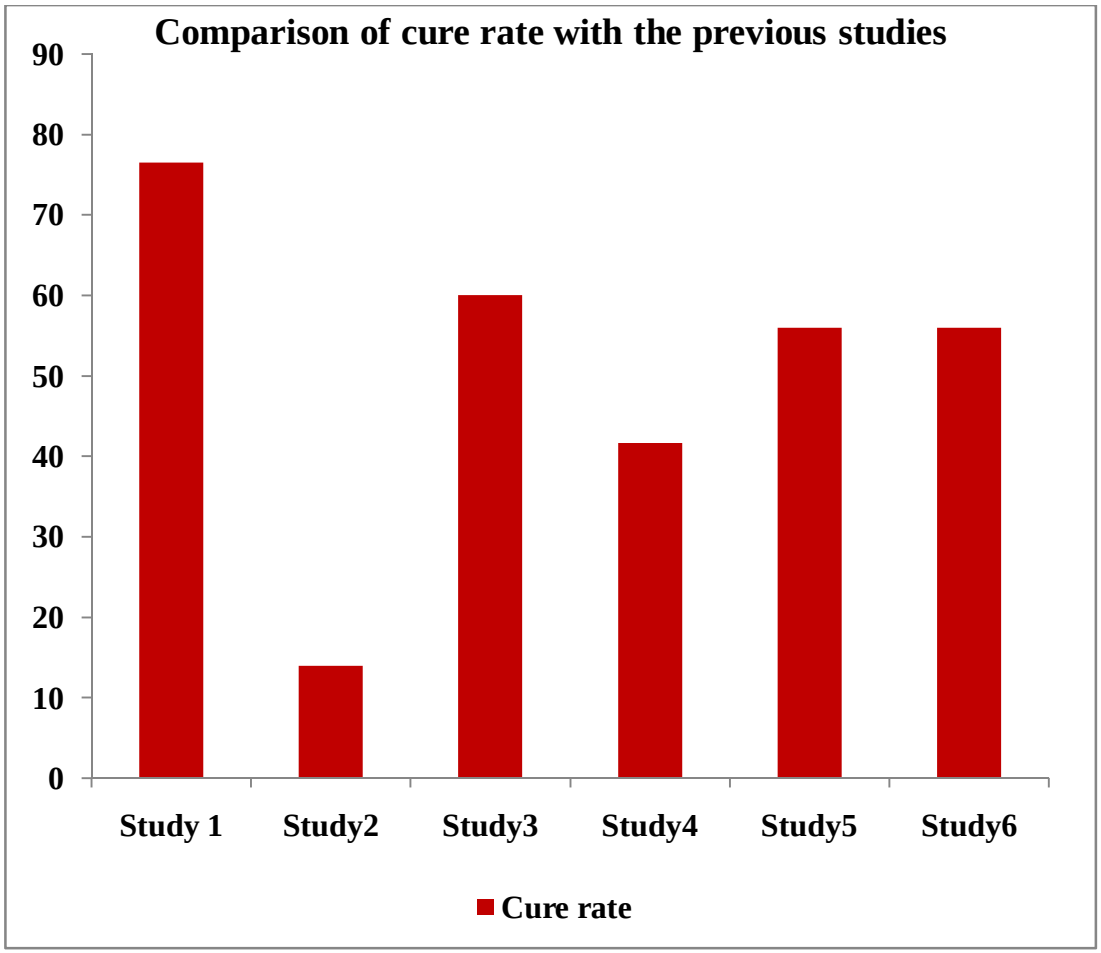



**Comparison of cure rate of cryotherapy group with previous studies**

The results of the cryotherapy group which is 56% obtained in our study, is lower than that of the a study which compared intralesional bleomycin and cryotherapy in the treatment of warts done by S.B.Dhar, which was 76.5%, but higher than that in another study which compared cryotherapy with topical salycilic acid in the treatment of warts which was only 14%[79,80] . A few other studies which compared cryotherapy with duct taping, cantharidin and fig tree showed showed the cure rates of cryotherapy to be 60%, 41.7% and 56% respectively[81,82,83].

## COMPARISON OF CURE RATE OF CRYOTHERAPY GROUP WITH PREVIOUS STUDIES

| Study Number | STUDY DONE BY | CURE RATE |
|---|---|---|
| 1. | Dhar.S.B – Cryotherapy versus intra lesional bleomycin | 76.5% |
| 2. | Sarah Cockayne – Cryotherapy versus topical salicylic acid | 14% |
| 3. | Focht.D.R – Cryotherapy versus duct taping | 60% |
| 4. | Kacar.N – Cryotherapy versus cantharidin-podophyllotoxin-salicylic acid | 41.7% |
| 5. | Bohlooli.S – Cryotherapy versus fig tree efficacy | 56% |
| 6. | Present study | 56% |


Comparison of cure rate with the previous studies
90
80
70
60
50
40
30
20
10
0
Study 1
Study2
Study3
Study4
Study5
Study6
Cure rate

## VII. TIME TAKEN FOR RESOLUTION:

In our study, the mean time taken for the resolution of warts by the cryotherapy group, was 2.28 weeks whereas that for the autoimplantation group was 6.64 which is statistically significant ( p = 0.002 ). So though the cure rate was higher in the autoimplantation group, the time taken for resolution is significantly longer when compared to the cryotherapy group.

Most of our patients (33) in the autoimplantation group showed complete clearance within 8 weeks and an earliest response at 3 weeks which are in accordance with the V.Shivakumar study of auto implantation therapy[3].

In the cryotherapy group, the minimum time taken for clearance of lesions was 1 week and the maximum time taken was 12 weeks.

## VIII. RECCURENCE :

The recurrence rate was 4% (2) in the cryotherapy group whereas in the autoimplantation group, there was no recurrence. Thus the recurrence rate was found to be significantly lower in the autpoimplantation group ($p = 0.0153 < 0.05$). The zero reccurence in the

autoimplantation group is comparable to the study on autoimplantation therapy by V.Shivakumar[3].

## IX. COMPLICATIONS :

Both the cryotherapy as well as the autoimplantation therapy had complications of their own. It was found that the complication rate was much higher in the cryotherapy group (20, 40%) as compared to the autoimplantation group (3,6%). In the autoimplantation group, 3 patients had complications of therapy. One patient had secondary infection at the autoimplantation site, and 2 patients developed an inflammatory nodule at the site of implantation of the wart. A few patients had transient hypopigmentation which disappeared in 2 weeks. These are in accordance with the complications noted in the Shivakumar study on auto implantation therapy for warts and the study on novel modification of the autoimplantation therapy for warts[3,68].

In the cryotherapy group, 20 out of the 50 patients experienced some kind of a complication like pain during and after the procedure, blistering, which was at times haemorrhagic, bleeding, hypopigmentation, hyperpigmentation, scarring and secondary infection. These complications were also noted in other studies which involved cryotherapy[80,81,82,83,84].

# CONCLUSION

1. The cure rate with homologous autoimplantation therapy for warts was significantly higher that the cure rate of cryotherapy with liquid nitrogen by the dipstick method. But the time taken for resolution was shorter by cryotherapy (Mean – 2.28 weeks) as compared to autoimplantation therapy (Mean – 6.46 weeks).

2. Complications were much higher in the cryotherapy group than the autoimplantation group. Both the procedures were safe and harmless as no severe complication was noted.

3. There was recurrence seen in the cryotherapy group whereas the autoimplantation group showed no recurrence, though the difference in the recurrence rate was not statistically significant

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# PROFORMA

Name : Age/Sex:

Hospital no.:

Occupation:

Address:

Socioeconomic status:

Complaints:

Duration-

Sites-

H/O contact-

Past history:

Treatment history:

Immunosuppressives –

Treatment for warts –

Personal history:

Smoker-

Alcoholic –

Risk of exposure to STD-

Drug addiction-

Diabetes mellitus-

Hypertension-

Family H/O warts:

General examination:

Dermatological examn.;

Skin : Sites-

Size/Type-

Surface-

Colour-

Koebner's phenomenon -

Mucous membrane –

Hair-

Nail-

Systemic examination : CVS –

RS –

P/A-

CNS-

Diagnosis :

Auto implantation done on :

Onset of resolution of lesions:

Disappearance of lesions :

Complications if any:

Investigations:

Haemogram- TC- DC-

ESR-

RBS –

Urea / Creat. –

HIV-

VDRL -

HBsAg –

Skin biopsy (if needed)-

Clinical photo :

1. Pre- treatment :
2. Post- treatment :

Consent :

# MASTER CHARTS
## GROUP - 1 (CRYOTHERAPY )

| SER No | Age | Sex | Duration | Occupation | Type | Sites | No. | H/O Rx | Result | Resolu. (WKS) | Recc. | Complic. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 29 | M | 24 | police | CW,PPW | 1,2 | 12 | 1 | C | 2 | N | N |
| 2 | 50 | M | 12 | labourer | CW | 1 | 8 | N | C | 4 | N | BL |
| 3 | 26 | F | 10 | teacher | CW | 2,5 | 9 | 2 | NC | - | N | PIG |
| 4 | 30 | M | 12 | mechanic | CW,PPW | 6,1,3,8 | 11 | 1 | C | 2 | N | BL |
| 5 | 42 | M | 8 | shopkeeper | CW | 1,2,3,4,6,7 | 20 | N | NC | - | N | N |
| 6 | 24 | M | 36 | company | CW | 2,5,6 | 10 | 1,2 | C | 8 | Y | N |
| 7 | 46 | F | 12 | housewife | CW | 6 | 7 | 2 | C | 2 | N | N |
| 8 | 12 | M | 10 | student | CW,PPW | 8 | 8 | 1 | C | 3 | N | PIG |
| 9 | 23 | M | 9 | company | CW,PPW | 2,3 | 14 | N | NC | - | N | N |
| 10 | 39 | F | 24 | housewife | CW,PPW | 1,3,4,8 | 16 | 3 | NC | - | N | N |
| 11 | 23 | M | 30 | company | CW | 2 | 9 | N | C | 10 | N | BL |
| 12 | 31 | M | 12 | teacher | CW | 1,2,4 | 21 | 2 | NC | - | N | N |
| 13 | 15 | F | 7 | student | PPW | 5 | 8 | 3 | C | 1 | N | N |
| 14 | 50 | M | 18 | labourer | PPW | 2,3,4,5 | 22 | N | NC | - | N | N |
| 15 | 14 | F | 11 | student | CW,PPW | 6,3,4 | 14 | 1,2 | C | 3 | N | N |
| 16 | 30 | M | 24 | driver | PPW | 1,2,7,8 | 16 | N | NC | - | N | PIG |
| 17 | 21 | F | 10 | student | CW | 1,2,7,8,10 | 31 | N | NC | - | N | N |
| 18 | 45 | M | 24 | police | PPW | 1,2 | 11 | 1,2,3 | C | 4 | N | N |
| 19 | 38 | F | 10 | receptionist | CW | 7,8 | 9 | 1 | C | 3 | N | BL,HYPO |
| 20 | 13 | F | 12 | student | CW | 2,10 | 12 | 1 | C | 5 | N | HYPOPIG |
| 21 | 27 | M | 12 | driver | PPW | 2 | 14 | N | NC | - | N | N |
| 22 | 16 | F | 8 | student | CW | 6,7,8 | 8 | 3 | C | 4 | N | N |
| 23 | 12 | M | 12 | student | PPW | 4 | 7 | 1,2 | C | 3 | N | HYPO |
| 24 | 25 | M | 24 | waiter | CW | 1,2,7,8 | 10 | N | NC | - | N | HYPO |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 25 | 42 | F | 12 | housewife | CW | 2,10 | 9 | N | C | 2 | N | N |
| 26 | 24 | M | 30 | doctor | CW | 1,2,4 | 13 | 1,2,3 | NC | - | N | BL |
| 27 | 15 | M | 7 | student | CW,PPW | 10 | 8 | 1 | C | 3 | N | N |
| 28 | 51 | M | 18 | labourer | PPW | 2,4,10 | 21 | N | NC | - | N | PIG |
| 29 | 23 | F | 18 | shopkeeper | CP,PPW | 1,2 | 10 | N | C | 12 | N | N |
| 30 | 47 | M | 6 | labourer | CW | 7 | 9 | N | C | 4 | N | N |
| 31 | 33 | M | 30 | typist | CW,PPW | 10 | 8 | N | C | 3 | N | PIG |
| 32 | 14 | F | 12 | student | CW | 3,7,8 | 11 | 1 | NC | - | N | HYPO |
| 33 | 21 | M | 8 | student | PPW | 6,2,3 | 16 | 1 | NC | - | N | N |
| 34 | 34 | F | 24 | housewife | CW,PPW | 2 | 9 | N | C | 4 | N | PIG |
| 35 | 36 | M | 12 | police | CW,PPW | 2,3,8 | 15 | 2 | NC | - | N | N |
| 36 | 44 | F | 10 | teacher | CW | 2,10 | 7 | 3 | C | 2 | N | BL |
| 37 | 19 | M | 18 | student | PPW | 2,4 | 12 | 1 | NC | - | N | N |
| 38 | 26 | M | 24 | mechanic | PPW | 2,4,10 | 10 | N | NC | - | N | BL |
| 39 | 39 | F | 18 | shopkeeper | CW | 6 | 9 | N | C | 4 | N | PIG |
| 40 | 13 | M | 6 | student | CW | 1,2,4 | 11 | 2 | NC | - | N | N |
| 41 | 30 | F | 7 | housewife | PPW | 2,10 | 19 | N | NC | - | N | N |
| 42 | 23 | M | 6 | doctor | CW | 2 | 8 | 2 | C | 3 | N | N |
| 43 | 17 | M | 11 | student | PPW | 7 | 9 | 3 | C | 4 | N | N |
| 44 | 50 | F | 12 | housewife | CW,PPW | 2 | 10 | N | C | 6 | N | N |
| 45 | 13 | M | 8 | student | CW,PPW | 2,4 | 12 | 3 | NC | - | N | N |
| 46 | 24 | F | 12 | steno | CW,PPW | 2,7,8 | 8 | 3 | C | 5 | Y | N |
| 47 | 22 | M | 12 | mechanic | CW | 6 | 21 | N | NC | - | N | N |
| 48 | 15 | M | 10 | student | CW | 6,2,3 | 20 | 3 | NC | - | N | HYPO |
| 49 | 57 | M | 30 | vendor | CW | 4 | 7 | N | C | 3 | N | BL |
| 50 | 42 | F | 12 | housewife | CW,PPW | 6 | 9 | 2 | C | 5 | N | N |

## GROUP II (AUTOIMPLANTATION)

| S. No | Age | Sex | Duration | Occupation | Type | Sites | No. | H/O Rx | Result | Resolu. (WKS) | Recc. | Complic. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 16 | M | 12 | student | CW | 1,2 | 8 | N | C | 10 | N | N |
| 2 | 60 | M | 10 | labourer | CW | 1,3 | 14 | 4 | C | 12 | N | N |
| 3 | 13 | M | 18 | student | PPW | 1,2,4 | 15 | 1,2 | C | 6 | N | HYPO |
| 4 | 12 | F | 36 | student | CW | 1,2 | 25 | N | C | 12 | N | N |
| 5 | 18 | M | 24 | mechanic | CW | 1 | 10 | 2 | C | 6 | N | N |
| 6 | 26 | F | 12 | company | CW | 1,2 | 8 | 2 | C | 12 | N | HYPO |
| 7 | 15 | M | 18 | student | CW | 1,3 | 12 | 1 | NC | - | N | N |
| 8 | 24 | M | 12 | driver | PPW | 1 | 6 | N | C | 5 | N | N |
| 9 | 25 | M | 36 | company | CW | 1,2 | 14 | 1,2 | NC | - | N | N |
| 10 | 28 | F | 18 | housewife | CW | 1 | 8 | 1 | C | 6 | N | N |
| 11 | 22 | M | 24 | technician | CW | 1,2 | 12 | 2 | NC | - | N | N |
| 12 | 26 | M | 12 | teacher | CW,PPW | 1,2,3 | 15 | N | C | 10 | N | N |
| 13 | 22 | F | 28 | steno | CW | 1 | 10 | 1 | C | 6 | N | N |
| 14 | 17 | M | 24 | supervisor | CW,PPW | 1 | 10 | N | NC | - | N | N |
| 15 | 51 | M | 24 | mechanic | CW,PPW | 1 | 8 | 4 | C | 12 | N | N |
| 16 | 25 | F | 12 | receptionist | CW | 1 | 6 | N | C | 6 | N | N |
| 17 | 21 | M | 12 | police | CW | 1 | 12 | 4 | C | 10 | N | N |
| 18 | 23 | M | 24 | student | CW,PPW | 1,2,4 | 10 | N | C | 12 | N | N |
| 19 | 21 | M | 18 | student | CW | 1,2,3,4 | 22 | N | NC | - | N | N |
| 20 | 16 | M | 12 | student | CW | 1,2 | 12 | N | C | 7 | N | N |
| 21 | 26 | M | 6 | operator | CW,PPW | 1,2 | 16 | 1 | NC | - | N | N |
| 22 | 23 | M | 24 | supervisor | CW,PPW | 1,2,3 | 10 | 2 | C | 9 | N | HYPO |
| 23 | 30 | M | 24 | driver | CW,PPW | 1,2,3 | 12 | 1,2 | NC | - | N | N |
| 24 | 26 | F | 12 | steno | CW | 1,2 | 8 | 3 | C | 4 | N | N |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 25 | 21 | M | 6 | supervisor | CW | 1 | 6 | N | C | 6 | N | N |
| 26 | 19 | M | 24 | salesman | CW,PPW | 1,2,3,4 | 20 | 4 | C | 7 | N | N |
| 27 | 22 | F | 24 | student | CW | 1,2 | 14 | N | C | 7 | N | N |
| 28 | 21 | M | 18 | student | CW | 1,2,3 | 18 | 1 | NC | - | N | N |
| 29 | 23 | M | 30 | office boy | CW,PPW | 1,2,3 | 12 | 3 | C | 7 | N | N |
| 30 | 19 | M | 6 | student | CW | 1 | 6 | N | C | 12 | N | N |
| 31 | 18 | M | 12 | student | CW | 1,2,3 | 15 | 2 | C | 11 | N | N |
| 32 | 17 | F | 30 | student | PPW | 1,2,3,6 | 20 | N | C | 3 | N | N |
| 33 | 12 | F | 6 | student | CW | 1,2,3 | 8 | 1 | C | 7 | N | N |
| 34 | 17 | M | 24 | student | CW | 1,2,3,6 | 18 | 1 | NC | - | N | N |
| 35 | 18 | F | 12 | receptionist | CW | 1,2 | 8 | N | C | 8 | N | N |
| 36 | 25 | F | 6 | housewife | CW | 1,2 | 6 | N | C | 8 | N | N |
| 37 | 21 | M | 24 | student | PPW | 1,3 | 8 | 1 | C | 8 | N | N |
| 38 | 36 | M | 12 | labourer | CW | 1,2,3 | 12 | N | C | 10 | N | N |
| 39 | 30 | M | 18 | labourer | CW | 1,2 | 8 | N | C | 12 | N | N |
| 40 | 18 | M | 6 | student | CW | 1,2,3 | 10 | N | C | 6 | N | N |
| 41 | 13 | F | 12 | student | PPW | 1,2 | 6 | N | C | 8 | N | N |
| 42 | 41 | M | 12 | driver | CW | 1,2,3 | 10 | N | C | 11 | N | N |
| 43 | 18 | M | 8 | student | CW | 1,2,3,4 | 12 | N | NC | - | N | N |
| 44 | 29 | M | 18 | waiter | CW,PPW | 1,2 | 6 | N | C | 8 | N | N |
| 45 | 32 | F | 12 | supervisor | CW,PPW | 1,2,6 | 8 | 1 | C | 10 | N | N |
| 46 | 27 | M | 6 | salesman | CW | 1,2,3 | 12 | N | C | 9 | N | N |
| 47 | 32 | M | 18 | technician | PPW | 1,2 | 12 | 1,2,3 | NC | - | N | N |
| 48 | 43 | F | 12 | housewife | CW | 1,2 | 14 | N | C | 6 | N | N |
| 49 | 21 | M | 6 | student | CW | 1 | 8 | N | C | 10 | N | N |
| 50 | 19 | M | 24 | student | CW,PPW | 1,2,4 | 10 | 1,2 | C | 12 | N | N |

# KEY TO MASTER CHART

| | | |
|---|---|---|
| M | – | Male |
| F | – | Female |
| CW | – | Common wart |
| PPW | – | Palmoplantar wart |
| DURATION | – | Duration of warts in the patient |
| NO. | – | Number of warts |
| C | – | Cured |
| NC | – | Not cured |
| N | – | No |
| COMPLIC | – | Complications |
| RESOLU. | – | Time taken for resolution in weeks |
| RECC. | – | Recurrence of warts |
| BL | – | Bleeding |
| PIG | – | Pigmentation |
| P | – | Pain |
| H/O RX | – | History of treatment |

1. Cryotherapy
2. Electrosurgery
3. Native medicine

SITES

1. Fingers

2. Dorsum of hands
3. Hands
4. Forearms
5. Arms
6. Feet
7. Legs & thighs
8. Trunk
9. Face
10. Neck
11. Scalp

**INSTITUTIONAL ETHICS COMMITTEE**
**MADRAS MEDICAL COLLEGE, CHENNAI -3**

Telephone No : 044 25305301
Fax : 044 25363970

**CERTIFICATE OF APPROVAL**

To
Dr. Suganthy V
PG in MDDVL
Madras Medical College, Chennai -3

Dear Dr. Suganthy V

The Institutional Ethics committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled "Treatment of multiple wartsefficacy of homologous autoimplantation therapy & comparison of homologous autoimplantation therapy Vs cryotherapy with liquid Nitroegen" No. 09122011

The following members of Ethics Committee were present in the meeting held on 22.12.2011 conducted at Madras Medical College, Chennai -3.

1. Prof. S.K. Rajan. MD -- Chairperson
2. Prof. R. Nandhini MD -- Member
   Director, Institute of Pharmacology ,MMC, Ch-3
3. Prof. Pregna B. Dolia MD -- Member
   Director , Institute of Biochemistry, MMC, Ch-3
4. Prof. S. Regunanthan, MD -- Member
   Prof of Internal Medicine, MMC, Ch-3
5. Prof. Md Ali MD. DM -- Member
   Prof & Head , Dept. of MGE, MMC,Ch-3
6. Thiru. S. Govindsamy. BA BL -- Lawyer

We approve the proposal to be conducted in its presented form.

Sd/ Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee